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Index

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Soeben erschien:

LEHRBUCH
DER
GERICHTLICHEN MEDIZIN

von

J. Dettling, Bern — S. Schönberg, Basel — F. Schwarz, Zürich

VIII + 552 Seiten und 134 Abbildungen sFr. 52.—

Aus dem Vorwort:

Beim Ende des letzten Weltkrieges waren praktisch sämtliche Lehrbücher dieses Faches innerhalb des deutschen Sprachgebietes verschwunden. Die Nachfrage sowohl bei Studierenden als auch bei Ärzten und Juristen war sehr groß. Daher haben die Autoren damals den Entschluß gefaßt, nach sorgfältiger Vorarbeit ein neuzeitliches Lehrbuch herauszubringen. Aber nicht nur der Mangel an guten klassischen Werken erforderte die Neuschaffung eines Lehrmittels, sondern mehr noch die großen Fortschritte, welche die Gerichtsmedizin in den letzten Dezennien zu verzeichnen hatte, und das ständige Steigen der Anforderungen, welche in mannigfacher Hinsicht an sie gestellt werden. Es sei nur an die gewaltige Zunahme des Verkehrs und damit auch der Unfälle gedacht, die zahlreichen Maßnahmen und gesetzlichen Bestimmungen zur Verringerung der Gefahren, die Rolle des Alkohols bei der Unfallsauslösung. Auch die enorme Entwicklung der chemischen Wissenschaft und Industrie hat den Gerichtsmediziner vor immer größere Aufgaben gestellt. Es sei auch erinnert an die Bedeutung der Blutuntersuchung zur Entscheidung in Vaterschaftsfragen, Blutgruppen, Rhesusfaktor, eine Forschung, die durch ihre Ergebnisse heute in der Rechtsprechung allgemein fest verankert ist.

Aus dem Inhalt:

Allgemeine gerichtliche Medizin – Die forensisch-medizinischen Wirkungsmittel – Die Basis der ärztlichen Wirksamkeit: Stellung als diplomierter Arzt; die Gesetze – Das ärztliche Geheimnis; Berufsgeheimnis; Berufspflicht; Falsches ärztliches Zeugnis; Ärztliche Anzeigepflicht – Allgemeine Grundsätze für die Erstellung von ärztlichen Zeugnissen und Gutachten – Die Lehre vom Gutachten – Der außerordentliche Todesfall – Die Leichenerscheinungen – Der plötzliche Tod aus natürlicher Ursache – Der Selbstmord in der gerichtlichen Medizin.

Spezielle gerichtliche Medizin – Allgemeine Gesichtspunkte für die Beurteilung von Körperverletzungen und Übersicht der medizinischen Aufgaben – Die Schnittverletzungen – Die Stichverletzungen – Hiebwunden bei schneidenden Objekten – Die stumpfe Gewalt – Die Quetschung – Die Gewebszerreißung – Schartenspuren – Der Automobilunfall – Motorrad- und Velounfälle – Todesfälle auf dem Eisenbahntrasse – Flugzeugunfälle – Absturz – Die Schußverletzungen – Tod und Gesundheitsschädigung durch abnorm hohen und abnorm tiefen Luftdruck – Schädigung durch abnorm hohe und abnorm tiefe Temperaturen – Der elektrische Unfall – Hungerkrankheiten und Hungertod – Der Tod durch gewaltsame Erstickung – Die Kindestötung – Fragen der Schwangerschaft, Geburt und Fruchtabtreibung – Gerichtlichmedizinische Untersuchungen bei Sexualdelikten.

Gerichtlich-medizinische Spurenkunde einschließlich Blutgruppen.

Die Toxikologie im Rahmen der gerichtlichen Medizin.

BASEL (Schweiz) S. KARGER NEW YORK

Demnächst erscheint:

Lehrbuch der Haut- und Geschlechtskrankheiten

von Prof. Dr. W. LUTZ – Basel

ca. 600 Seiten und 450 Abbildungen – Preis ca. Fr. 60.—

AUS DEM VORWORT: Der Ausarbeitung dieses Lehrbuchs lag der Leitgedanke zugrunde, eine systematisch aufgebaute Darstellung der Haut- und Geschlechtskrankheiten von einem einheitlichen Gesichtspunkt aus und nach einheitlichen Richtlinien zu geben; in der Absicht, dem Leser einerseits den Überblick über das gesamte Gebiet zu erleichtern und ihm andererseits eine Klassifikationsmöglichkeit zu bieten, innerhalb derer er im Laufe der Studien erworbene weitere Kenntnisse leicht einzuordnen und damit nutzbringend zu verwenden vermag.

Daß infolge der Kompliziertheit des Stoffes im Hinblick auf eine dermatologische Systematik eine Lücke besteht, wird seit jeher zugegeben, und Versuche, sie zu überbrücken, sind ja schon mehrfach unternommen worden. Ohne weiteres ist klar, daß ein systematischer Aufbau nur von einer ätiologisch-pathologischen Grundlage aus erfolgen kann. Diesem Prinzip ist bei den durch eine einheitliche Ursache erzeugten Dermatosen leicht zu entsprechen. Diejenigen Krankheitsbilder dagegen, die in der gleichen, klinisch gut umschriebenen Form durch die allerverschiedensten Ursachen ausgelöst werden, sowie diejenigen, klinisch ebenfalls durchaus charakteristischen Dermatosen, über deren Ätiologie und Genese wir vorerst nur wenig oder noch nichts Sicheres wissen, bieten einer Erfassung von einem einheitlichen Gesichtspunkt aus sehr große Schwierigkeiten.

Beim Versuch einer Lösung dieses Problems geht das Lehrbuch von der Konzeption der réactions cutanées durch Louis Brocq aus. Sie erscheint uns als eine geeignete Grundlage, um die Dermatosen dieser beiden letztgenannten Gruppen zunächst nach dem von F. von Hebra eingeführten Prinzip in ihren klinischen Erscheinungen scharf zu umschreiben und dann im Anschluß daran die teils bekannten, teils vermuteten ätiologischen und pathogenetischen Faktoren, deren wesentliche Grundlagen im allgemeinen Teil zu skizzieren sind, zu analysieren, mit dem klinischen Bild in Vergleich zu setzen und zur Diskussion zu stellen.

Diese Anordnung ermöglicht es, die Beschreibung der Krankheitsbilder verhältnismäßig knapp zu fassen und die theoretischen Fragen im einzelnen nur kurz anzudeuten, da sie schon aus der Gesamtanlage deutlich hervorgehen sollten. Sie dürfte nicht nur einfache Tatsachen und Hypothesen aufzählen, sondern auch Anregungen zur weiteren Vertiefung in die vielen noch offenen Probleme geben. Die häufigeren Dermatosen werden natürlich etwas ausführlicher und besonders vom praktischen Gesichtspunkt aus dargestellt, die selteneren und exotischen kürzer erwähnt. Es wurde eine möglichst vollständige Anführung der bekannt gewordenen Hautleiden angestrebt. Dem Studierenden wird damit vielleicht ein etwas zu weit gefaßter Stoff vorgelegt, doch wird er ihm ohne Schwierigkeiten das für seinen Bedarf Notwendige entnehmen können; dem Allgemeinpraktiker und wohl auch dem jüngeren Dermatologen dagegen dürfte es nicht unerwünscht sein, eine Zusammenstellung zur Verfügung zu haben, in der er wenigstens schlagwortweise eine ihn im Moment interessierende Frage oder Affektion erwähnt und gruppiert findet.

Durch das reiche Bildmaterial bildet das Buch gleichzeitig auch einen Atlas.

BASEL (Schweiz) S. KARGER NEW YORK

Travail de la Clinique Ophtalmologique de l'Université de Genève
(Directeur Professeur A. Franceschetti)

RECHERCHES DE MARQUEURS DE CHROMOSOMES DANS UNE FAMILLE ATTEINTE DE RÉTINITE PIGMENTAIRE DOMINANTE[1])

par A. RYWLIN

Etant donné la grande rareté de la dégénérescence pigmentaire de la rétine à hérédité dominante, il nous a semblé utile de publier l'arbre généalogique d'une famille Fa.–De. que nous avons eu l'occasion d'observer. En outre, nous avons recherché, chez les membres atteints et indemnes, les caractères héréditaires qui nous servent de marqueurs de chromosomes (*Kloepfer*, *Franceschetti* [a]), dans l'espoir que notre étude, ajoutée à d'autres travaux orientés dans le même sens, apportera un jour des éléments suffisants permettant de mieux se prononcer sur la localisation des gènes pathologiques autosomiques.

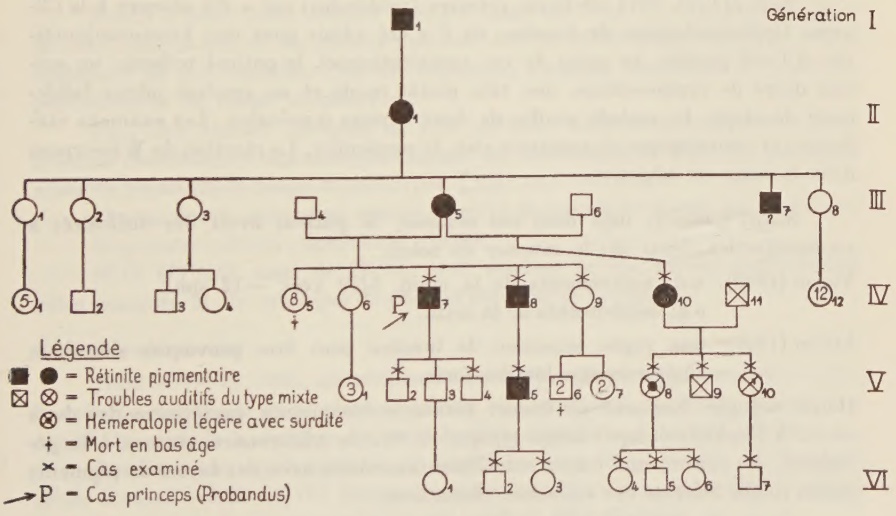

Fig. 1. Arbre généalogique de la famille Fa.-De.

[1]) Travail fait dans le Service de Génétique de la Clinique, sous la direction du Dr *D. Klein*.

Recherches généalogiques et cliniques (Fig. 1).

En ce qui concerne les trois premières générations de la famille Fa., nous avons pu reconstituer l'arbre généalogique grâce à des données anamnestiques et aux informations fournies par les bureaux communaux.

Première génération:

H. (*I/1*), originaire du Jura neuchâtelois, était connu dans les environs parce qu'il était devenu aveugle. Il est très probable qu'il s'agissait d'une *rétinite pigmentaire.*

Deuxième génération:

H. P. (*II/1*), voyait mal la nuit; est morte aveugle. *Rétinite pigmentaire* très probable.

Troisième génération:

Lina P. (*III/5*), 1843—1887, voyait mal la nuit. Il s'agissait très probablement d'une *rétinite pigmentaire.* Quatre de ses soeurs (III/1, 2, 3, 8) voyaient toutes bien, et parmi leur descendance nous n'avons pas pu déceler de dégénérescence pigmentaire de la rétine. Un frère, *Alexis P.* (III/7), aurait eu une *mauvaise vue.* Il est mort sans avoir eu d'enfant. Nous n'avons pas pu préciser le diagnostic.

Quatrième génération:

I. F. (*IV/6*), 1872–1932, est morte en France. Elle aurait toujours eu une bonne vue.

E. F. (*IV/7*), 1873 est le *cas princeps* (*probandus*) qui a été observé à la Clinique Ophtalmologique de Genève, où il a été admis pour une kératoconjonctivite à l'oeil gauche. Au point de vue constitutionnel, le patient présente un certain degré de cyphoscoliose, une tête plutôt ronde et un système pileux faiblement dévelopé. Le malade souffre de deux hernies inguinales. Les examens otologique et neurologique ne montrent rien de particulier. La réaction de Wasserman dans le sang est négative.

Status oculaire: déjà dans son enfance, le patient avait des difficultés à reconnaître les objets dès le coucher du soleil.

Vision (1940): o.d. mouvements de la main, 5/50 avec —12 sph.
o.g. mouvements de la main.

Vision (1949): une vague sensation de lumière peut être provoquée des deux côtés avec une lumière forte.

Haute myopie. Segment antérieur: cataracte compliquée postérieure des deux côtés. A l'ophtalmoscope: *image typique de rétinite pigmentaire,* surtout à la périphérie. Au centre, une importante lésion maculaire avec des foyers de pigments plutôt ronds. Sclérose des vaisseaux choroïdiens.

Charles F., (*IV/8*), 1877, retraité à l'âge de 50 ans parce que sa vue avait trop baissé. Au point de vue constitutionnel: tête plutôt ronde, légère scoliose de la colonne vertébrale, système pileux peu développé. Les autres status ne présentent rien de particulier.

Status oculaire: déjà à l'âge de 8–10 ans, ses camarades lui disaient qu'il avait des „yeux de poule", parce qu'il ne voyait plus bien dès la tombée de la nuit. Vision: sensation lumineuse des deux côtés lorsqu'on emploie une lumière forte. Segment antérieur: début de cataracte des deux côtés. A l'ophtalmoscope, on observe une *rétinite pigmentaire typique* avec une certaine pigmentation de la région maculaire.

Rose S. (*IV/9*), 1880, ressemble au point de vue constitutionnel à ses deux frères. Tête ronde, légère cyphose. Les autres status n'ont rien de particulier. A l'âge de sept ans, elle a eu "une tâche à l'oeil gauche", et depuis lors, elle n'a jamais bien vu avec cet oeil. Il n'y a jamais eu d'héméralopie.

Status oculaire: o.d.: 0,2. o.g.: perçoit les mouvements des doigts. Les pupilles réagissent aux deux modes. L'oeil gauche diverge à la fin de la convergence. Début de cataracte prononcée aux deux yeux, plus forte à gauche qu'à droite. Fond de l'oeil: artères un peu rétrécies, à part cela sans altération des deux côtés.

Jeanne D., (*IV/10*), 1883, est une demi-soeur de cette fratrie (fille du deuxième mariage de la mère). Au point de vue constitutionnel: Tête plutôt ronde, légère scoliose.

Status oculaire (Clinique Ophtalmologique de Lausanne; Prof. Streiff): Vision o.d.: mouvements de la main à 10 cm.

o.g.: compte les doigts à 80 cm. 2/50. Astigmatisme myopique direct.

Motilité: léger strabisme divergent à l'oeil droit.

Cristallin: o.d. soucoupe postérieure avec iridescence et de nombreuses opacités en miettes de pain dans les couches profondes de la corticale postérieure.

o.g. Début de soucoupe postérieure avec des opacités en miettes de pain et en forme de rayons dans la corticale postérieure. Opacités punctiformes, poudreuses dans la corticale antérieure.

Fonds d'yeux: o.d.: difficile à voir à cause de l'état du cristallin. Atrophie du nerf optique qui est de couleur chamois. Artères extrêmement étroites, veines également un peu rétrécies. Près des vaisseaux, quelques rares amas de pigments partiellement en forme d'ostéocytes.

o.g.: bien visible. Atrophie du nerf optique. Artères extrêmement minces. Sclérose choroïdienne très marquée surtout du côté temporal. Près des vaisseaux, amas de pigments en forme d'ostéocytes. TAR: 40.

Champ visuel: nettement rétréci jusqu'au dessous de 10 degrés des deux côtés.

Diagnostic: *rétinite pigmentaire typique.*

M.D. (*IV/11*), mari de IV/10, avait souffert de son vivant d'une *surdité* assez marquée. Il n'y avait pas de parenté entre lui et sa femme.

Cinquième génération:

Jules F. (*V/2*), 1903, mécanicien de profession. Type athlétique, tête ronde, la colonne vertébrale et le système pileux sont normaux, le palais est étroit et ogival. Le malade a souffert de deux hernies inguinales dans son enfance.

Status oculaire: astigmatisme myopique des deux côtés. Vision: 1,0 des deux côtés, accepte —0,25 cyl/180 degrés. Segment antérieur: rien de particulier. Fond de l'oeil normal. Le patient n'a jamais souffert d'héméralopie.

Edouard F., (*V/3*), 1905, s'est suicidé au service militaire en 1939. Etait carabinier et garde-frontière. D'après les dires de sa famille, il voyait bien le jour et la nuit. Aurait pourtant eu une *hétérochromie.*

Henri F., (*V/4*), 1911, typographe de son métier, est mort en 1948 d'une affection pulmonaire. Il avait une vue tout à fait normale.

Gérald F., (*V/5*), 1917, est brachycéphale, présente une légère cyphose de la colonne vertébrale, système pileux peu développé, pas de trouble otologique.

Status oculaire: souffrait déjà à l'école d'héméralopie.

Vision o.d.: 1 avec —0,25 sph. et cyl. —0,5/0 degré.

o.g.: 1 avec —0,75 sph. et cyl. +1,0/105 degrés.

Le segment antérieur ne présente rien de particulier.

Fond de l'oeil: artères étroites, absence de pigmentation périphérique, choroïde pâle.

Champ visuel: o.d.: du côté temporal rétrécissement jusqu'à 70 degrés. Du côté nasal jusqu'à 25 degrés. En haut jusqu'à 10 degrés et en bas jusqu'à 15 degrés.

o.g.: du côté temporal rétrécissement jusqu'à 60 degrés, du côté nasal jusqu'à 20 degrés, et en haut et en bas jusqu'à 10 degrés.

Diagnostic: image typique de la *rétinite pigmentaire sans pigment* (Professeur Franceschetti).

V/6 et *V/7: enfants de Rose S.* (*IV/9*). Le premier, un garçon, est mort à l'âge de onze mois des suites d'une scarlatine. Le second, une fille, est bien portante et n'a jamais souffert d'héméralopie. Le troisième enfant, est un garçon qui est mort à l'âge de dix ans d'une péritonite. Le quatrième enfant, une fille, voit bien.

Yvonne B., (*V/8*), 1905, présente au point de vue constitutionnel une brachycéphalie et une légère cyphoscoliose.

Status neurologiquue: reflexes vifs des deux côtés.

Status oculaire: vision: 1,0 des deux côtés. P 2/30 avec + 0,75 des deux côtés. Se plaint d'avoir des difficultés à s'orienter la nuit, depuis 1930, environ. Segment antérieur: naevi pigmentaires de l'iris des deux côtés.

Fond de l'oeil: bord de la papille légèrement flou (à droite plus qu'à gauche). Artères de largeur normale. A l'extrême périphérie, quelques petits points blanchâtres.

Champs visuel: o.d.: du côté temporal, il y a un rétrécissement jusqu'à 60 degrés. Côté nasal normal. En bas et en haut il y a un très léger rétrécissement.

o.g.: champ visuel rétréci seulement du côté temporal à 60 degrés.

A l'examen d'adaptation (Clinique Ophtalmologique de Lausanne), la malade n'est jamais très sûre si elle voit ou non: „Je vois, je ne vois plus, je vois de nouveau", même si l'on ne change pas l'intensité lumineuse du disque. Il ne semble pas y avoir de grand déficit. La malade éprouve pourtant depuis 1930 une grande difficulté à s'orienter dès qu'apparaît l'obscurité.

Diagnostic: héméralopie légère.

Status otologique: (Clinique O-R-L, Genève, Prof. Montandon) L'examen de l'audiogramme montre que la conduction aérienne est plus fortement diminuée que la conduction osseuse. On peut donc conclure à une surdité du type *otosclérose avec une certaine atteinte de l'oreille interne.*

Hélène B., (*V/10*), 1910,

Status neurologique: réflexes vifs des deux côtés.

Status oculaire: vision 1,0 des deux côtés.

Status otologique: la malade se plaint d'une surdité assez marquée, qui aurait débuté lors de ses vingt ans. Il semble s'agir d'une *surdité de transmission*, mais un audiogramme n'a pas pu être fait.

V/1, les trois enfants de *I. F.*, *IV/6*, qui vivent en France, voient bien d'après les renseignements donnés par la famille.

Sixième génération:

Charles André F., (*VI/2*), 1945, ne présente rien de pathologique aux différents status. Il aurait pourtant souffert à sa naissance d'une hernie ombilicale et d'une hernie inguinale des deux côtés.

Micheline F., (*VI/3*), 1947, a souffert d'une hernie inguinale gauche à sa naissance. On ne trouve rien de pathologique aux autres status.

Simone B., (*VI/4*), 1935,

Status oculaire: vision: 1,5 des deux côtés. Segment antérieur et fond de l'oeil sans altération.

Status otologique: malade présentant une surdité de transmission à l'oreille gauche. A l'otoscopie, elle présente une cicatrice dans la partie postéro-supérieure du tympan gauche.

Albert B., (*VI/5*), 1936,

Status oculaire: vision o.d.: 1,25 – o.g.: 1,0. Le segment antérieur est sans particularité. Fond de l'oeil: la papille gauche est plus petite que la papille droite, et montre un petit halo pigmentaire du côté temporal supérieur. Champ visuel, adaptation au scotopticomètre, normaux.

Le status otologique et les autres status ne présentent rien de particulier.

Denise B., (*VI/6*), 1939.

Status oculaire: vision: o.d. 3/50, voit 0,1 avec — 2,50. o.g.: 1,25, accepte sph + 1,25. Fixe avec l'oeil gauche. Strabisme convergent concommitant à l'oeil droit. Le segment antérieur ne présente rien de particulier. Fond de l'oeil: sans altération, sauf une petite pigmentation dans le secteur temporal de la papille droite.

Champ visuel: o.d. légèrement rétréci de tous les côtés, surtout du côté temporal. o. g.: normal. L'adaptation est normale, pas d'héméralopie.

Diagnostic: strabisme convergent concommitant à l'oeil droit. Anisométrie: myopie de l'oeil droit, hypermétropie de l'oeil gauche.

Albert B., (*VI/7*), 1945, ne présente rien de pathologique à l'examen des différents status.

Résumé.

Dans cinq générations successives, il y a huit personnes atteintes, cinq hommes et trois femmes, dont quatre ont pu être examinés. Trois parmi eux (IV/7, 8, 10) présentent le tableau clinique d'une rétinite pigmentaire typique. Le quatrième (V/5) présente une rétinite pigmentaire sans pigment. Il y a, en plus, un cas (V/8) d'héméralopie légère avec surdité due à une otosclérose. Cette association résulte de la rencontre accidentelle de deux gènes. La maladie est transmise deux fois par des hommes et trois fois par des

femmes. L'anamnèse, quand elle a pu être faite, a montré que dans tous les cas l'héméralopie débuta dans l'enfance et était progressive. Il n'y a pas d'anticipation. Il n'y a pas de consanguinité.

Il est indiqué maintenant d'énumérer brièvement les différents modes de transmission de la dégénérescence pigmentaire de la rétine, et de voir lequel d'entre eux correspond le mieux à l'arbre généalogique décrit plus haut. La dégénérescence pigmentaire de la rétine peut se transmettre soit selon un mode autosomique, soit selon un mode gonosomique.

Transmission autosomique:

a) *Le mode récessif* est le plus fréquent. En effet, la consanguinité des parents, qui est un des critères principaux de l'hérédité récessive, se trouve fréquemment dans les familles atteintes de dégénérescence pigmentaire de la rétine. On la trouve selon *Bell*, dans le 27,2 % des cas. D'autre part, l'affection apparaît très souvent chez plusieurs enfants d'un couple indemne, et le rapport entre le nombre des enfants atteints et le nombre des enfants indemnes correspond à peu près au chiffre théorique de 1:3.

b) *Le mode dominant*, d'après *Groenouw*, se voit dans le 3,1 % des cas. Selon d'autres auteurs ce chiffre varie entre 3,1 % et 6,7 %. Il ne faut parler de dominance que si la maladie est transmise de génération en génération pendant plus de deux générations, afin d'éviter les cas de pseudo-dominance (croisement de retour de *Mendel*). Il faut rappeler aussi qu'une dominance autosomique ne peut être affirmée que lorsqu'il y a transmission du père au fils, puisque une dominance liée au sexe (voir plus loin) peut simuler une dominance autosomique. Lorsque dans un arbre généalogique, par ailleurs dominant, on voit une génération indemne, on parle de dominance irrégulière.

Dans notre arbre généalogique, il semble s'agir d'une dominance simple, étant donné que:

1. Chaque personne atteinte a un parent atteint.
2. La maladie se manifeste successivement dans cinq générations.
3. Les membres indemnes de la famille ne transmettent pas la maladie.
4. Il n'y a pas de consanguinité dans la famille.
5. Il y a une transmission du père au fils (IV/8 à V/5).

En Suisse, 4 arbres généalogiques de dégénérescence pigmentaire dominante de la rétine ont été publiés jusqu'à présent. *Tobler-Berg* publia le cas d'une famille avec une rétinite pigmentaire atypique transmise par trois générations. Il y avait 8 atteints dont 5 hommes et 3 femmes. Pour un autre membre masculin dans cette famille la présence de la maladie n'était pas sûre. L'héméralopie a été progressive, ce qui apporte un argument contre la théorie de *Fleischer*, d'après laquelle l'héméralopie dans les cas dominants serait toujours congénitale et stationnaire. *Heuscher*, *Gysin* et *Hegner* ont décrit une famille avec trois générations successives atteintes. En tout, il y avait onze membres atteints dont 5 hommes et 6 femmes. On trouve des formes transitoires de la maladie, allant de la forme typique de pigmentation, aux formes frustes (Rétinite pigmentaire sans pigment).

Dans le cas de *Rehsteiner*, la maladie se transmet dans 4 générations successives. Il y a 16 membres atteints, dont 7 hommes et 9 femmes. Il y a 33 membres de la famille bien portants, et 21 qui n'ont pas été examinés. Il s'agit d'une rétinite pigmentaire typique. Il est intéressant de noter que la pigmentation apparaît nettement avant que l'acuité visuelle, le champ visuel et l'adaptation à l'obscurité soient atteints.

Franceschetti et *Klein* ont publié l'arbre généalogique d'une famille atteinte de dégénérescence pigmentaire de la rétine à hérédité dominante irrégulière, et d'une surdité familiale due à une otosclérose. Ce qui est intéressant dans ce cas, c'est que l'on assiste à une transformation du gène récessif en gène dominant, ce qui pourrait s'expliquer par la théorie de *Beckerhaus* qui prétend que la forme dominante est due à l'intervention d'un facteur complémentaire s'associant au facteur principal.

Il faut se demander, en ce qui concerne la dégénérescence pigmentaire de la rétine à hérédité dominante, s'il faut la considérer comme une entité à mettre à part de la forme récessive. *Beckerhaus* n'a pas trouvé de différence ophtalmoscopique entre la forme récessive et la forme dominante. Il ne croit pas qu'il s'agisse de deux maladies différentes. Il admet tout simplement un changement de valence du gène. *Fleischer* estime qu'il s'agit de deux formes différentes, la forme dominante étant essentiellement une héméralopie congénitale stationnaire, à laquelle s'ajoute un déplacement de pigment qui donne cliniquement un aspect ressemblant beaucoup à celui de la forme récessive.

Franceschetti (b) ne croit pas que la dégénérescence pigmentaire de la rétine à hérédité dominante soit essentiellement différente de la forme récessive, puisqu'on trouve plusieurs modes de transmission héréditaire dans beaucoup de maladies dégénératives. *Allan* prétend que la forme dominante étant due à une forme génotypique hétérozygote, est beaucoup moins grave que la forme récessive qui est due à une formule homozygote. La forme récessive liée au sexe occuperait une place intermédiaire en ce qui concerne la gravité. Notre étude des cas de dégénérescence pigmentaire de la rétine à hérédité dominante, ne nous permet pas de nous ranger aux conclusions d'*Allan* en ce qui concerne la différence de gravité de ces affections. Il y a cependant une différence nette entre la forme récessive et la forme dominante. Ainsi l'association d'autres tares héréditaires à la forme dominante est beaucoup plus rare qu'à la forme récessive. *Wibaut*, parmi 300 malades souffrant de la forme dominante de la dégénérescence pigmentaire de la rétine, a trouvé chez un seul une maladie mentale. Il croit que cette association est purement accidentelle. Il en est ainsi pour le cas V/8 (fig. 1) de notre arbre généalogique. Le gène responsable pour l'otosclérose est introduit par IV/11 qui vient d'une famille tout à fait indépendante de la famille atteinte de dégénérescence pigmentaire de la rétine. Un cas analogue a été publié par *Allan*. Il s'agit d'un cas atteint à la fois de dégénérescence pigmentaire de la rétine à hérédité dominante et d'idiotie. Dans ce cas la rétinite pigmentaire est transmise par le père qui vient d'une famille de rétinite pigmentaire dominante, tandis que l'idiotie est transmise par la mère qui en est elle-même indemne, mais qui vient d'une famille souffrant d'une idiotie à transmission récessive liée au sexe. Il s'agirait donc d'une ségrégation indépendante de deux gènes.

Par contre, dans les formes récessives, *Wibaut* a pu montrer grâce à des méthodes statistiques, que l'association à la surdité n'était pas une combinaison due au hasard. Selon lui, c'est un gène à effet polyphène qui serait responsable de la tare associée.

Transmission gonosomique:

a) *Le mode récessif lié au sexe* est rare. En effet, d'après *Franceschetti*, on ne trouve dans toute la littérature jusqu'en 1930 qu'un arbre généalogique de dégénérescence pigmentaire de la rétine dans lequel ce mode de transmission puisse être admis avec certitude. Il s'agit d'un arbre généalogique publié d'abord par *Nettleship*, puis par *Usher*, et classé dans l'oeuvre de *Bell* sous le numéro 156. Dans

quatre générations, il y a six hommes atteints et l'affection et toujours transmise par des femmes indemnes. Par la suite, en 1931, *Gasalla* publia l'arbre généalogique d'une famille dans laquelle, pendant deux générations, il n'y a que des hommes atteints, l'affection étant toujours transmise par des femmes indemnes. Les enfants d'hommes atteints sont indemnes. En 1935, *McQuarrie* a décrit un arbre généalogique présentant cinq générations où l'on trouve 21 hommes atteints et une femme aveugle, qui n'a d'ailleurs pas pu être examinée. En 1937, *Allan* a publié un arbre généalogique de deux générations dans lequel il y a quatre hommes atteints. La maladie est transmise par une femme indemne.

Bell, en examinant tous les cas de dégénérescence pigmentaire de la rétine publiés jusqu'en 1922, trouve que 55,6 % sont du sexe masculin. Selon d'autres auteurs, ce chiffre varie entre 54 et 70 %. D'autre part, *Nettleship* a trouvé que pour 50 mères qui transmettent la maladie, il n'y a que 36 pères qui en font autant. Il n'est pas exclu que l'excès d'hommes atteints et la transmission plus fréquente par les femmes soient en rapport avec le fait que dans les statistiques générales, un certain nombre de familles avec une rétinite pigmentaire récessive liée au sexe est pris en considération. Cette hypothèse est corroborée par *Wibaut* qui a trouvé que l'excès d'atteints mâles se voyait surtout dans les formes récessives. En effet, dans 26 arbres généalogiques dominants, *Wibaut* trouve 148 hommes atteints pour 149 femmes atteintes, tandis que sur 264 arbres généalogiques récessifs, il a trouvé 317 hommes atteints contre 235 femmes atteintes. Cependant, la rareté des familles avec un mode de transmission récessif lié au sexe permet de penser également à une autre explication. Ainsi, l'excès d'hommes atteints pourrait être dû à une influence du sexe sur la manifestation phénotypique. D'autre part, la transmission plus fréquente de la maladie par les femmes pourrait être expliquée par une certaine sélection sociale, dans ce sens que les hommes atteints de rétinite pigmentaire sont plus „handicapés" que les femmes et ne se marient souvent pas.

b) *Le mode dominant lié au sexe* peut, comme nous l'avons dit plus haut, simuler une transmission dominante autosomique. Dans notre cas, ce mode est exclu, puisqu'il y a une transmission du père au fils (Fig. 1, IV/8 à V/5).

c) *Le sex-linkage intermédiaire*, qui a été décrit indépendemment par *Goedbloed* et *Waardenburg* pour la choroïdérémie, pourrait

être en cause au cas de dégénérescence pigmentaire de la rétine. *Falls* et *Conermann* ont vu récemment une famille dans laquelle les hommes présentaient une forme sévère et progressive de dégénérescence pigmentaire de la rétine, tandis que les femmes hétérozygotes présentaient une forme légère, l'image ophtalmoscopique rappelant les „drusen" de la lame de *Bruch*.

d) *Le sex-linkage incomplet* ne peut être mis en évidence que par des méthodes statistiques qui ont été décrites par *Haldane* en 1936. Cet auteur a attiré l'attention sur le fait que certaines affections pouvaient être dues, malgré l'apparence d'une transmission dominante ou récessive simple, à un sex-linkage incomplet. Dans ces cas, le gène pathologique siègerait soit dans la partie homologue du chromosome X, soit dans la partie homologue du chromosome Y, selon qu'il a été transmis par la mère ou par le père. Si ce gène est dominant, on trouvera avant tout des enfants atteints qui seront du même sexe que le grand-parent paternel atteint.

La fréquence relative des enfants atteints du sexe opposé et des enfants normaux du sexe correspondant au grand-parent paternel atteint, nous permettra de calculer la valeur du crossing-over. Pour le gène récessif, on peut faire des calculs semblables en classant les enfants normaux et atteints selon le sexe de leur grand-parent paternel conducteur. *Haldane* suggère par des moyens statistiques que 40 % des gènes responsables de la dégénérescence pigmentaire de la rétine à hérédité dominante, sont liés incomplètement au sexe avec une valeur de crossing-over de 33 %.

Franceschetti (c), en ajoutant aux 17 familles étudiées par *Haldane*, celle de *Hanhart*, a trouvé que la fréquence du crossing-over pour les formes récessives, était égale à $0{,}32 \pm 0{,}045$. La différence entre ce chiffre et 0,5 est de 0,18, c'est-à-dire 4 fois plus grande que l'erreur moyenne, donc probante.

Il faut donc se demander s'il ne s'agit pas dans notre arbre généalogique, malgré l'apparence d'une dominance simple, d'un sex-linkage incomplet. La méthode ingénieuse de *Haldane*, appliquée à cet arbre généalogique seul, ne donne pas de résultats concluants, parce que les chiffres sont trop petits. Nous avons par conséquent assorti notre arbre généalogique à d'autres cas d'apparence dominante afin de les soumettre à cette analyse statistique. Tous ces arbres généalogiques sont ultérieurs à l'oeuvre de *Bell* de 1922, et n'ont pas été utilisés dans le travail de *Haldane*.

Les résultats de notre analyse, se basant sur 9 cas de la littérature et sur notre arbre généalogique, sont résumés dans les tableaux accompagnants (Fig. 2).

Fig. 2.

Enfants d'hommes qui ont hérité la rétinite pigmentaire de leur *père.*

Arbre généalogique	Père	Atteints		Normaux	
		m.	f.	m.	f.
Rehsteiner	II/2	0	2	1	0
Hassels	III/3	1	1	4	2
	III/17	3	1	0	1
	III/21	2	1	1	2
	IV/34	0	0	3	3
Tobler-Berg	II/10	1	0	1	1
Allan 1944	IV/92	0	0	2	2
1938 (no 1)	II/7	3	2	3	1
	III/10	0	1	1	0
	III/13	1	1	2	2
	III/17	0	0	1	0
Scheurlen (no 7)	IV/2	1	0	0	0
François	III/9	2	0	0	1
Total		14	9	19	15

Enfants d'hommes qui ont hérité la rétinite pigmentaire de leur *mère.*

Arbre généalogique	Père	Atteints		Normaux	
		m.	f.	m.	f.
Rehsteiner	III/15	0	1	1	3
Hassels	IV/2	1	1	1	0
	V/11	2	0	1	1
Allan 1944	III/2	3	1	2	3
	III/3	1	1	3	1
	III/5	2	0	2	3
1938 (no 2)	II/5	1	3	3	1
Scheurlen (no 6)	II/2	0	2	0	1
(no 7)	III/2	1	0	1	0
Rieger	III/4	0	0	1	1
	III/8	2	1	0	0
cas personnel	IV/7	0	0	3	0
	IV/8	1	0	0	0
Total		14	10	18	14

Nous trouvons donc:

Du sexe correspondant au grand-parent paternel atteint:

Atteints : 24
Normaux: 33

Du sexe opposé au grand-parent paternel atteint:

Atteints : 23
Normaux: 33

La valeur du crossing-over est donc égale à

$$\frac{33 + 23}{33 + 24 + 33 + 23} = \frac{56}{113} = 0{,}495 \pm 0{,}047$$

La différence entre 0,495 et 0,50, valeur théorique pour une hérédité autosomique, est de 0,005, chiffre plus petit que l'erreur moyenne et donc non significatif. Nous n'avons donc pas trouvé, dans l'analyse de ces arbres généalogiques, un indice parlant en faveur d'un sex-linkage incomplet. Par contre, les arbres généalogiques étudiés par *Haldane* suggèrent, selon lui, que 40 % des gènes responsables de la dégénérescence pigmentaire à hérédité dominante se transmettent d'après un sex-linkage incomplet.

Puisque la présence d'une sex-linkage incomplet n'a pas pu être mise en évidence, nous avons estimé utile de rechercher les „marqueurs de chromosomes", afin de contribuer à un matériel qui permettra un jour d'établir un linkage entre le gène de la rétinite pigmentaire et un gène autosomique.

Nous avons recherché les facteurs suivants, et d'après *Kloepfer* et *Franceschetti* nous les groupons comme suit:

Caractère	*Positif*	*Négatif*
1. Antigène A	Présent	Absent
2. Antigène B	Présent	Absent
3. Antigène M	Présent	Absent
4. Antigène N	Présent	Absent
5. P.T.C.	Positif	Négatif
6. Pilosité digitale	Présente	Absente
7. Tourbillon	à droite	à gauche
8. Forme de cheveux	Frisés	Plats
9. Teinte de cheveux	Foncés	Clairs
10. Cheveux roux	Présents	Absents
11. Lobule de l'oreille	Collé	Décollé
12. Taille de l'oreille	Grande	Petite
13. Position du pavillon	Collé	Décollé
14. Yeux bleus	Absents	Présents

Caractère	*Positif*	*Négatif*
15. Strabisme	Présent	Absent
16. Langue	Curler	Non-curler
17. Verrues, naevi	Présents	Absents
18. Longueur des doigts	Annulaire plus long	Index plus long
19. Handedness	Droitier	Gaucher
20. Sexe	Masculin	Féminin
21. Oeil conducteur	Droit	Gauche
22. Anomalie dentaire	Présente	Absente
23. Anomalie des ongles	Présente	Absente
24. Facteur rhésus	Positif	Négatif

La figure 3 présente un tableau synoptique des marqueurs de chromosomes tels que nous les avons trouvés dans la famille Fa. – De.

Fig. 3.

Génération	IV	IV	IV	IV	V	V	V	V	V	V	VI	VI	VI
Numéro	7	8	9	10	2	4	5	8	9	10	4	5	6
1. Antigène A	—	—	—	—	—	+	—	—	+	+	—	—	—
2. Antigène B	—	+	+	—	—	—	—	—	—	—	—	—	—
3. Antigène M	+	+	+	+	+	+	+	+	+	+	+	+	+
4. Antigène N	—	+	+	+	+	+	+	+	+	+	—	—	+
5. P.T.C.	+	—	+	+	+	+	—	—	+	+	—	—	+
6. Pilosité digitale	—	—	—	—	+	a	—	—	+	—	—	—	—
7. Tourbillon	b	—	+	—	—	a	—	—	b	—	+	+	+
8. Forme des cheveux	—	—	—	—	—	a	—	—	—	—	—	—	—
9. Teinte des cheveux	+	+	+	+	+	a	+	+	+	+	—	—	—
10. Cheveux roux	—	—	—	—	—	a	—	—	—	—	—	—	—
11. Lobule de l'oreille	+	+	+	+	—	a	—	+	+	+	+	+	—
12. Taille de l'oreille	+	+	+	+	+	a	+	+	+	+	+	+	+
13. Position du pavillon	c	+	+	+	+	a	+	+	+	+	+	+	+
14. Yeux bleus	+	+	+	+	+	a	+	+	+	+	+	+	—
15. Strabisme	—	—	—	—	—	a	—	—	—	—	—	—	+
16. Langue	—	—	+	—	+	a	+	—	+	—	—	+	+
17. Verrues, naevi etc.	—	—	—	—	—	a	—	—	+	—	—	—	—
18. Longueur des doigts	+	+	+	+	+	a	+	c	c	+	—	c	+
19. Handedness	+	+	+	+	+	a	+	+	+	+	+	+	+
20. Sexe	+	+	—	—	+	+	+	—	+	—	—	+	+
21. Oeil conducteur	d	d	+	d	+	a	+	+	+	+	+	+	—
22. Anomalie dentaire	—	e	—	e	—	a	e	—	—	—	—	—	—
23. Anomalie des ongles	—	—	—	—	—	a	—	—	—	—	—	—	—
24. Facteur rhésus	—	+	+	+	+	a	+	+	+	+	—	+	+

Figure 3. Marqueurs de chromosomes chez la famille Fa. — De.

Légende: a = pas examiné à cause de décès; b = calvitie; c = membre droit +, membre gauche —; d = aveugle; e = prothèse.

Selon *Penrose* et d'autres, quand on veut déceler si oui ou non il y a linkage, en employant la méthode élaborée par lui („sib-pair method"), il faut au moins examiner 100 paires pour pouvoir émettre une conclusion. L'arbre généalogique publié plus haut (Fig. 1) est donc insuffisant pour faire ces calculs. Nous avons pu trouver dans la littérature, un travail de *Tertsch* contenant 12 arbres généalogiques de dégénérescence pigmentaire de la rétine avec une détermination des groupes sanguins AOB. Six autres arbres généalogiques de dégénérescence pigmentaire de la rétine ont été mis à notre disposition par la Clinique Ophtalmologique de Genève. Les groupes sanguins ont été déterminé dans ces cas.

Nous sommes ainsi arrivés à avoir 114 paires. Il faut pourtant dire que, dans ce groupe, il s'agit d'un mélange de cas récessifs et dominants. En comparant la dégénérescence pigmentaire de la rétine avec l'antigène A, nous avons trouvé que la proportion des doubles concordants et discordants par rapport aux couples avec concordance pour un seul caractère, est de 62:52, ce qui montre une déviation en faveur du linkage. Pour voir s'il s'agissait d'une différence significative au point de vue statistique, nous avons appliqué la méthode du χ^2. Dans ce cas le $\chi^2 = 2{,}29$, ce qui correspond à une probabilité entre 0,10 et 0,20. La prépondérance des doubles concordants et discordants n'est donc pas significative. En comparant la dégénérescence pigmentaire de la rétine avec l'antigène B, selon la „Sib-method", nous avons trouvé que la proportion des doubles concordants et discordants par rapport aux couples avec concordance pour un seul caractère, est de 59:55. Il y a donc une petite déviation dans le sens d'un linkage, mais qui n'est pas significative. En effet, le $\chi^2 = 0{,}46$; la probabilité correspondante à cette valeur est égale à 0,50. *Ce résultat parle contre la présence du gène de la rétinite pigmentaire dans le chromosome qui est porteur des gènes déterminant les groupes sanguins AOB.*

Résumé.

Description de l'arbre généalogique d'une famille atteinte de dégénérescence pigmentaire de la rétine à hérédité dominante. Dans cinq générations successives, il y a huit personnes atteintes, dont quatre ont pu être examinées. Trois parmi eux (IV/7, 8, 10) présentent le tableau clinique typique. Le quatrième, V/5, est atteint d'une rétinite pigmentaire sans pigment. Il y a en plus, un cas d'héméralopie

légère avec surdité due à une otosclérose. Cette association est le résultat d'une rencontre accidentelle de deux gènes. La maladie est transmise deux fois par des hommes et trois fois par des femmes. L'héméralopie a été progressive. Il n'y a pas d'anticipation et pas de consanguinité. Ajoutant à notre cas neuf arbres généalogiques publiés après 1922, nous les avons soumis à une analyse statistique concernant la théorie de *Haldane* sur l'hérédité incomplète liée au sexe. Nous n'avons pas trouvé d'indice en faveur d'un sex-linkage incomplet.

Les marqueurs de chromosomes ont été recherchés chez tous les membres examinés de la famille. Un calcul de linkage a été fait pour la rétinite pigmentaire avec l'antigène A et l'antigène B. Le résultat parle contre un linkage entre les gènes en question.

Summary.

The predigree of a family with pigmentary degeneration of the retina due to dominant genes is described. During 5 consecutive generations there were 8 persons with the disease, of whom 4 could be examined. 3 of them (IV/7, 8, 10) showed the typical clinical picture. The fourth, V/5, had a retinitis without pigmentation. Besides there was one case suffering from slight hemeralopia and from deafness because of otosclerosis. This combination seems to be the result of an accidental meeting of two genes. The disease was transferred two times by men and three times by women. Thehemeralopia was progressive. There was no "anticipation" and no consanguinity. To our cases we added 9 pedigrees published after 1922 and analysed them statistically according to Haldane's theory of incomplete sex-linked inheritance. We did not find any indication of incomplete sex-linked inheritance.

The chromosome markings were examined in all the members of the family. A calculation of linkage in regard to the antigen A and the antigen B was made for the pigmentary retinitis. The result speaks against linkage between the genes in question.

Zusammenfassung.

Beschreibung des Stammbaumes einer Familie, welche erblich von Pigmentdegeneration der Netzhaut befallen ist. In fünf aufeinanderfolgenden Generationen befinden sich acht betroffene Personen, von denen vier befragt werden konnten. Drei von ihnen weisen das typische klinische Bild auf. Der vierte ist von einer Entzündung der Netzhaut befallen, welcher das Pigment jedoch fehlt. Es findet sich

ein weiterer Fall von leichter Hämäralopie verbunden mit Taubheit, hervorgerufen durch eine Otosklerose. Diese Verbindung ist wahrscheinlich das Ergebnis eines zufälligen Zusammentreffens der beiden Gene. Die Krankheit ist zweimal durch Männer, und dreimal durch Frauen übertragen worden. Die Hämäralopie ist fortschreitend gewesen. Ein früheres Vorkommen in den späteren Generationen oder eine Verwandtschaft existieren nicht. Unserem Fall haben wir neun nach 1922 veröffentlichte Stammbäume hinzugefügt und einer statistischen Analyse unterzogen entsprechend der Theorie von Haldane von der an das Geschlecht gebundenen, unvollständigen Erblichkeit. Ein Anzeichen zu Gunsten einer unvollständigen Geschlechtsbindung hat sich nicht gefunden. Die Chromosommarkierungen sind bei allen befragten Angehörigen der Familie untersucht worden. Eine Kuppelungsberechnung der Pigmententzündung der Netzhaut ist mit dem Antigen A und dem Antigen B durchgeführt worden. Das Ergebnis spricht gegen eine Kuppelung zwischen den in Frage kommenden Genen.

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THE FORMAL LOGIC OF THE NATURE NURTURE ISSUE

by LANCELOT HOGBEN, F. R. S.

1. Semantics of Nature and Nurture.

Recorded variation of a population is exhaustively and exclusively classifiable from a biological viewpoint in terms of: (a) *nature*, i. e. differences inherent in the composition of one or both gametes which contribute to the make-up of different individuals; (b) *nurture*, i. e. all external circumstances contributory to the development of the fertilised egg, including circumstances inherent in the uterine milieu of a species which is viviparous; (c) errors of observation. In *Nature and Nurture* (1933) *Hogben* advanced reasons for the view that the hope of evaluating the respective contributions of nature and nurture to variation within a genotypically heterogeneous population in an environment which is not uniform is illusory in virtue of the highly complex and diverse relations between environmental differences and the magnitude of manifest differences attributable to gene substitutions. The experimental work of *Gordon* and *Sang* (1941) reinforces the arguments embodied in Hogben's schematic *Nature-Nurture Indicator* diagram. The question we have set ourselves to answer in what follows is: how far can the statistical procedure denoted by the expression analysis of variance make it possible to separate the observed total variance of a population into components uniquely attributable to one or the other.

It will sidestep some of the semantic pitfalls which beset the discussion of nature and nurture, if we first ask: in what sense are we entitled to ascribe a unique meaning to the components of such a balance sheet of variance? In this context, our concern is with a population of different genotypes exposed to variable conditions of development. The assertion that such and such a fraction of total variance is due to heredity then signifies that we should reduce the total variance of the population by that amount if we were able to replace all constituent individuals by individuals of one and the

same (*the standard*) genotype. Likewise, the assertion that such and such a fraction is attributable to environment is referable to what reduction of total variance would result from exposure of the same assemblage of individuals of diverse genotypes to one and the same (*standard*) external conditions.

In the absence of arbitrary qualification of one sort or another, the first assertion has *no unique meaning* unless it is also permissible to assert that the choice of the standard genotype is immaterial, i. e. that the range and dispersion of variability of every constituent genotype is identical within the prescribed framework of external differences. The second assertion has no unique meaning unless we can also legitimately declare that the choice of the standard environment is immaterial in the sense that the range and dispersion of variability of the prescribed mixed population is the same within a homogeneous environment regardless of how we eliminate the relevant environmental variables.

Each such assertion implies that nature and nurture exert an influence on population structure independently, i. e. that there is *no interaction*. Only in so far as there is no interaction, are we free to postulate the dual system of strictly additive factors implicit in the rationale of the procedure we are about to examine. Thus *Churchill Eisenhart* uses the term *interaction* as biologists also use it in connexion with the nature-nurture issue, when he remarks that "when additivity does not prevail, we say that there are interactions between row and column factors."

Having defined the sense in which we can appropriately associate a component of population variance with a particular source, it is still necessary to get into focus what information about sources of variation is or is not implicit in the *taxonomic framework* of a particular experimental design. With appropriate experimental precautions, the familiar lay-out of varieties by columns and treatments by rows (or *vice versa*) can be one of which we are entitled to postulate one criterion of classification as exclusively genetic, the other being exclusively environmental. A necessary qualification to this claim is the need to culture each variety in one and the same environment before the beginning of the test to ensure that unequal response to treatment is not due to previous experience. With such safeguards, the lay-out of the experiment entitles us to seek answers to questions about the effects of the *particular set of external variables* specified by the row-class criterion and the *particular set of genotypes* identified

by the column-class criterion. Other genetic and other environmental differences may contribute to variation from cell to cell in the two dimensional grid of score values, being indistinguishable in a single experiment from residual sources of variation attributable to error of observation alone.

Every additional criterion of environment or genetic variability not implicit in the initial framework calls for further elaboration of the design of the experiment. Hence any assessment of the overall contribution of nature or the overall contribution of nurture to total variance can be at best a good approximation, and then only as the result of repeated exploration of new sources of variability. In short, exact assessment of the total contribution of nature or that of nurture implies both the absence of interaction and a taxonomic framework which comprehensively specifies all classes of relevant variables of either sort inherent in the set-up to which it refers.

Whatever we may legitimately say for or against the use of analysis of variance *vis-à-vis* the nature-nurture issue, it is therefore clear that its legitimate terms of reference do not extend to an exhaustive breakdown in the sense that it can isolate a residual component due to *error of observation alone*. It would be trite to say this, if it were less easy to cite enquiries purporting to establish the trivial role of nurture with respect to differences of I. Q. in school populations on the basis of observations exclusively classified in accordance with the investigator's preconception of what external circumstances are favourable to variability.

That there exists some confusion concerning the legitimate uses of the *Analysis of Variance* scarcely calls for surprise. For the overwhelming majority of biological research workers who invoke its use derive their knowledge from manuals setting forth appropriate schemata for computation by reference to exemplary material without exhibiting either the logical assumptions or mathematical operations pertinent to its credentials and hence to its applicability to an actual situation. As pointed out by *Churchill Eisenhart* (1947), handbooks in current use employ the expression somewhat indiscriminately to manipulations of three sorts:

(a) evaluation of summarising indices which are tautologies of any assemblage of numbers set out grid-wise;

(b) evaluation of ratios with a view to testing for homogeneity;

(c) presentation of a balance sheet exhibiting components of variance each uniquely attributable to a particular source.

The realisability of (b) and (c) necessarily stands or falls with certain assumptions concerning the distribution of the variates involved; and the appeal of such assumptions depends less on the availability of empirical information to justify them than—in the word of the author last cited—"the more general nature of the inferences that may be drawn". Writing as a mathematician, *Churchill Eisenhart* examines the logical assumptions underlying the analysis of variance within the technical framework of the understanding that mathematical postulates advanced for the reason stated are valid. Accordingly, many biologists who might otherwise, and with advantage, take cognisance of the conclusions he puts forward may fail to grasp their implications. It is our aim to clarify the logic of the several operations denoted by analysis of variance without introducing mathematical postulates whose relevance to the theory arises only in the domain of significance and/or confidence. This we shall be able to do by recourse to an economical notation the meaning of which we can visualise at every stage by recourse to statistical models.

2. *Tautologies of the score grid.*

In a grid-wise lay-out for a 2-way or 3-way classification of numbers certain relations between mean sums of square deviations are necessarily true, and have no intrinsic relation to causality or to statistical theory in the ordinary sense of the term. It will simplify our task if we recognise this at the outset. The accompanying schema (Table II) exhibits the relevant parameters when our concern is with 2 criteria of classification. The grid (Table I) of r rows and c columns has rc cells to each of which we assign a score. We denote as x_{ij} the score of the cell in the column whose rank is i and row whose rank is j. Three operative symbols suffice to express all these relations compactly

$$\frac{1}{rc}\sum_{j=1}^{j=r}\sum_{i=1}^{i=c}(\ldots) \equiv \mathrm{E}(\ldots) \equiv \frac{1}{rc}\sum_{i=1}^{i=c}\sum_{j=1}^{j=r}(\ldots)$$

$$\frac{1}{r}\sum_{j=1}^{j=r}(\ldots) \equiv \mathrm{E}_r \qquad \textit{and} \qquad \frac{1}{c}\sum_{i=1}^{i=c}(\ldots) \equiv \mathrm{E}_c$$

In this notation we may therefore write:

$$\mathrm{E}_r.\mathrm{E}_c(\ldots.) \equiv \mathrm{E}(\ldots.) \equiv \mathrm{E}_c.\mathrm{E}_r(\ldots.) \qquad (2.1)$$

Table I.

	i = 1	i = 2	....		....	i = c
j = 1	x_{11}	x_{21}	....	x_{i1}	....	x_{c1}
j = 2	x_{12}	x_{22}	....	x_{i2}	....	x_{c2}
...	....	....	....	...	....	...
	x_{1j}	x_{2j}	....	x_{ij}	....	x_{cj}
...	....	....	....	....	....	....
j = r	x_{1r}	x_{2r}	....	x_{ir}	....	x_{cr}

Table II.

	Mean of	Variance
Whole grid	$M = \frac{1}{cr} \sum_{i=1}^{i=c} \sum_{j=1}^{j=r} x_{ij}$	$\frac{1}{rc} \sum_{i=1}^{i=c} \sum_{j=1}^{j=r} (x_{ij} - M^2) = V$
Within-row (*j*th) scores	$M_j = \frac{1}{c} \sum_{i=1}^{i=c} x_{ij}$	$\frac{1}{c} \sum_{i=1}^{i=c} (x_{ij} - M_j)^2 = V_j$
Within-column (*i*th) scores	$M = \frac{1}{r} \sum_{j=1}^{j=r} x_{ij}$	$\frac{1}{r} \sum_{j=1}^{j=r} (x_{ij} - M_i)^2 = V_i$
Row Means	$M = \frac{1}{r} \sum_{j=1}^{j=r} M_j$	$\frac{1}{r} \sum_{j=1}^{j=r} (M_j - M)^2 = V(M_r)$
Column Means	$M = \frac{1}{c} \sum_{i=1}^{i=c} M_i$	$\frac{1}{c} \sum_{i=1}^{i=c} (M_i - M)^2 = V(M_c)$

The items of Table II then become

	Mean	Variance
Whole Grid	$E(x_{cr}) = M$	$E(x_{cr}^2) - M^2 = V = E(x_{cr} - M)^2$
Within-row scores	$E_c(x_{cr}) = M_r$	$E_c(x_{cr}^2) - M_r^2 = V_r = E(x_{cr} - M_r)^2$
Within-col. scores	$E_r(x_{cr}) = M_c$	$E_c(x_{cr}^2) - M_c^2 = V_c = E(x_{cr} - M_c)^2$
Row means	$E_r(M_r) = M$	$E_r(M_r^2) - M^2 = V(M_r) = E_r(M_r - M)^2$
Column means	$E_c(M_c) = M$	$E_c(M_c^2) - M^2 = V(M_c) = E_c(M_c - M)^2$.

By analogy with the customary form of the expressions $V(M_c)$ and $V(M_r)$ we may write without ambiguity the mean within-row and mean within-column variances for the grid as a whole as

$$E_r(V_r) = M(V_r) \qquad \textit{and} \qquad E_c(V_c) = M(V_c).$$

If E_o signifies any one of the three operators in (2. 1) the following rule of thumb defines a simultaneous change of scale and origin, A and k being constants:

$$E_0(A.x_{cr} + k) = A.E_0(x_{cr}) + k \tag{2.2}$$

The following identities are implicit in (2. 1) and (2. 2):

$$E_c(M_r) = M_r \qquad \textit{and} \qquad E_r(M_c) = M_c \tag{2.3}$$

$$E(M_c.x_{cr}) = E_c\left[M_c.E_r(x_{cr})\right] = E_c(M_c^2) \tag{2.4}$$

$$E(M_r.x_{cr}) = E_r\left[M_r.E_c(x_{cr})\right] = E_r(M_r^2) \tag{2.5}$$

$$E(M.x_{cr}) = M.E(x_{cr}) = M^2 \tag{2.6}$$

$$E(M_r.M_c) = E_r\left[M_r.E_c(M_c)\right] = E_r(M_r.M) = M^2 \tag{2.7}$$

$$E(M.M_c) = M^2 = E(M.M_r) \tag{2.8}$$

The fundamental tautologies of the 2-dimensional grid fall out of this notation immediately as follows:

$$\begin{aligned} M(V_r) &= E_r.E_c(x_{cr}^2) - E_r(M_r^2) = E(x_{cr}^2) - E_r(M_r^2) \\ &= V + M^2 - E_r(M^2) = V - \left\{E_r(M_r^2) - M^2\right\} \\ &= V - V(M_r) \end{aligned}$$

$$\therefore \quad M(V_r) + V(M_r) = V$$

Similary

$$M(V_c) + V(M_c) = V$$

$$\therefore M(V_r) + V(M_r) = V = M(V_c) + V(M_c) \qquad (2.9)$$

We shall later use a parameter V_z defined alternatively in virtue of (2.9) as:

$$M(V_c) + M(V_r) - V = V_z = V - V(M_c) - V(M_r) \qquad (2.10)$$

By recourse to (2.3) — (2.8), it is easy to show that

$$E(x_{cr} - M_r - M_c + M)^2 = V_z \qquad (2.11)$$

For rapid computation of the foregoing grid parameters the grand total of scores and of square scores together with the squares of the row totals and column totals suffice in accordance with the following schema:

$$T = \sum_{i=1}^{i=c} \sum_{j=1}^{j=r} x_{ij} \; ; \; T_i = \sum_{j=1}^{j=r} x_{ij} \; ; \; T_j = \sum_{i=1}^{i=c} x_{ij}$$

$$rc.S = T^2 ; r.S_c = \sum_{i=1}^{i=c} T_i^2 \; ; \; c.S_r = \sum_{j=1}^{j=r} T_j^2 \; ; \; S_q = \sum_{i=1}^{i=c} \sum_{j=1}^{j=r} x_{ij}^2$$

We then have:

$$rc.V = S_q - S \qquad (2.12)$$

$$rc.V(M_c) = S_c - S \qquad (2.13)$$

$$rc.V(M_r) = S_r - S \qquad (2.14)$$

$$rc.V_z = S_q - S_c - S_r + S \qquad (2.15)$$

Whence also:

$$rc.M(V_c) = S_q - S_c \quad \textit{and} \quad rc.M(V_r) = S_q - S_r$$

When our concern is with three criteria of classification, we can visualise operations comparable to the foregoing by recourse to the laminated grid of n layers in fig. 1. We then denote the cell score of layer h, column i and row j as x_{hij}, the total number (ncr) of cells in the grid being distributed thus:

Layers rc	Row slabs nc	Column slabs nr
Pillars n	Rows c	Columns r

We then retain the symbols E_r and E_c with the same meaning as heretofore for *within-layer* operations, but shall need the additional symbol

$$E_n(\ldots.) = \frac{1}{n} \sum_{h=1}^{h=n} (\ldots.) \qquad (2.16)$$

As before, we use $E(\ldots.)$ to signify the operation of extracting the mean value of *all* the appropriate items in the grid, so that in *any* order:

$$E(\ldots.) \equiv E_n.E_r.E_c(\ldots.) \equiv E_r.E_n.E_c(\ldots.) \textit{ etc.} \qquad (2.17)$$

To distinguish between operations involving one, two or three dimensions, we shall employ a dot notation. By P_x we signify a parameter of the whole grid (e. g. the total variance V_x). By addition of n, r or c respectively after a dot we signify that the parameter refers to one of n layers, one of r row-slabs or one of c column-slabs. By addition of rc, nr or nc respectively we identify it accordingly with one of rc pillars, one of nr rows or one of nc columns. Table III gives the code, to which it is only necessary to add:

$$E_c.E_r(V_{x.rc}) = M(V_{x.rc});\ E_r(V_{x.r}) = M(V_{x.r});\ E_c(V_{x.c}) = M(V_c)$$

Corresponding to the 2 identities of the 2-dimensional grid specified by (2.9) we may now formulate 12 with respect to the solid score grid. Since each layer, row slab or column slab is itself a 2-dimensional, the following six call for no comment, being implicit in (2.9):

Within-layers :

$$E_c(V_{x.cn}) + E_c(M_{x.cn} - M_{x.n})^2 = V_{x.n} = E_r(V_{x.rn}) + E_r(M_{x.rn} - M_{x.n})^2 \qquad (2.18)$$

Within row-slabs :

$$E_n(V_{x.rn}) + E_n(M_{x.rn} - M_{x.r})^2 = V_{x.r} = E_c(V_{x.rc}) + E_c(M_{x.rc} - M_{x.r})^2 \qquad (2.19)$$

Within column-slabs :

$$E_n(V_{x.cn}) + E_n(M_{x.cn} - M_{x.c})^2 = V_{x.c} = E_r(V_{x.rc}) + E_r(M_{x.rc} - M_{x.c})^2 \qquad (2.20)$$

Other results follow from the possibility of rearranging the grid cells. We may put the nc cells of each row slab end to end to make a 2-dimensional grid whose total variance is V_x. This grid has still r rows of nc cells and nc columns of r cells, the row variance being $V_{x.r}$ and row mean $M_{x.r}$. Accordingly, we have the row-slab identity:

Table III.

	Means	Variance of cell scores *within*	Variance of *Means of*
ars	$M_{x.cr} = E_n(x_{h.cr})$	$E_n(x^2_{h.cr}) - M^2_{x.cr} = V_{x.cr}$ $= E_n(x_{h.cr} - M_{x.cr})^2$	$E_r.E_c(M_{x.cr} - M)^2 = V(M_{x.cr})$ $= E_r.E_c(M^2_{x.cr}) - M^2$
v	$M_{x.rn} = E_c(x_{i.nr})$	$E_c(x^2_{i.nr}) - M^2_{x.nr} = V_{x.nr}$ $= E_c(x_{i.nr} - M_{x.nr})^2$	$E_n.E_r(M_{x.nr} - M)^2 = V(M_{x.nr})$ $= E_n.E_r(M^2_{x.nr}) - M^2$
umn	$M_{x.cn} = E_r(x_{j.nc})$	$E_r(x^2_{j.nc}) - M^2_{x.nc} = V_{x.nc}$ $= E_r(x_{j.nc} - M_{x.nc})^2$	$E_n.E_c(M_{x.nc} - M)^2 = V(M_{x.nc})$ $= E_n.E_c(M^2_{x.nc}) - M^2$
ver	$M_{x.n} = E_r.E_c(x_{ij.n})$ $(= E_r.M_{x.nr} = E_c.M_{x.nc})$	$E_r.E_c(x^2_{ij.n}) - M^2_{x.n} = V_{x.n}$ $= E_c.E_r(x_{ij.n} - M_{x.n})^2$	$E_n(M_{x.n} - M)^2 = V(M_{x.n})$ $= E_n(M^2_{x.n}) - M^2$
v-slab	$M_{x.r} = E_c.E_n(x_{hi.r})$ $(= E_n.M_{x.nr} = E_c.M_{x.cr})$	$E_c.E_n(x^2_{hi.r}) - M^2_{x.r} = V_{x.r}$ $= E_c.E_n(x_{hi.r} - M_{x.r})^2$	$E_r(M_{x.r} - M)^2 = V(M_{x.r})$ $= E_r(M^2_{x.r}) - M^2$
umn slab	$M_{x.c} = E_r.E_n(x_{hj.c})$ $(= E_n.M_{x.nc} = E_r.M_{x.cr})$	$E_r.E_n(x^2_{hj.c}) - M^2_{x.c} = V_{x.c}$ $= E_r.E_n(x_{hj.c} - M_{x.c})^2$	$E_c(M_{x.c} - M)^2 = V(M_{x.c})$ $= E_c(M^2_{x.c}) - M^2$
ole Grid	$M = E(x_{hij})$ $(= E_c.M_{x.c} = E_c.E_n.M_{x.nc}$ *etc*$)$	$V = E(x^2_{hij}) - M^2$ $= E(x_{hij} - M)^2$	....

$$E_r(M_{x.r} - M_x)^2 + E_r(V_{x.r}) = V_x$$

If we put the nr cells of a column in single file we can make a grid of c columns, with column variance $V_{x.c}$, the mean being $M_{x.c}$. Again the total variance is V_x, whence the *column-slab* identity:

$$E_c(M_{x.c} - M_x)^2 + E_c(V_{x.c}) = V_x$$

If we lay out the rc cells of a layer as a single row, we may make a grid of n rows with row variance $V_{x.n}$ *etc.*, whence the *layer* identy:

$$E_n(M_{x.n} - M_x)^2 + E_n(V_{x.n}) = V_x$$

Finally, we may derive the following relation between pillars:

$$E_r.E_c(M_{x.rc} - M_x)^2 = E_r.E_c(M^2_{x.rc}) - 2M_x.E_r.E_c(M_{x.rc}) + M^2_x$$
$$= E_r.E_c(M^2_{x.rc}) - M^2_x$$

$$E_r.E_c(V_{x.rc}) = E_r.E_c.E_n(x^2_{ncr}) - E_r.E_c(M^2_{x.rc})$$

$$\therefore\ E_r.E_c(M_{x.rc} - M_x)^2 + E_r.E_c(V_{x.rc}) = E(x^2_{ncr}) - M^2_x = V_x$$

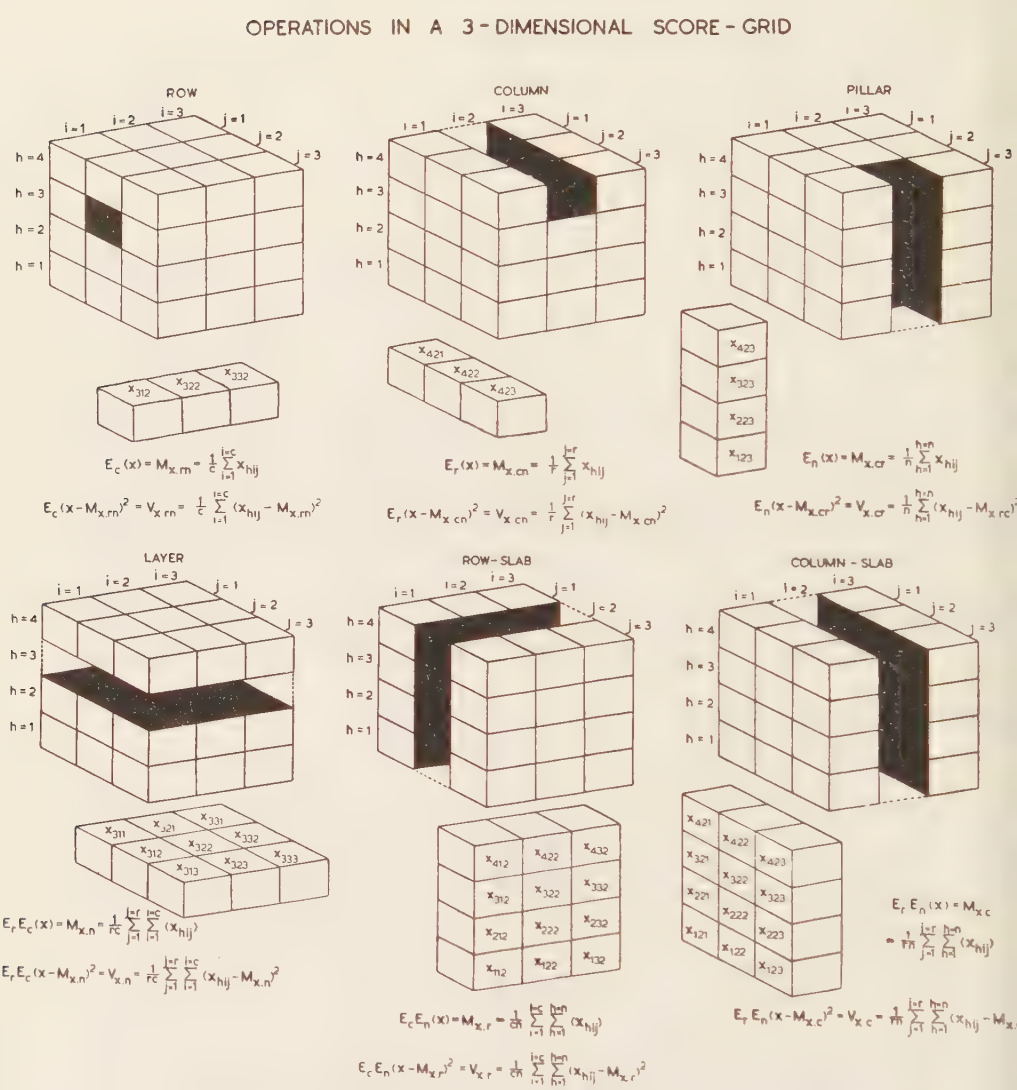


Fig. 1. The 3-dimensional Score-grid.

We may write the four identities last derived without ambiguity as

$$\mathrm{V}\,(\mathrm{M}_{\mathrm{x.r}}) + \mathrm{M}\,(\mathrm{V}_{\mathrm{x.r}}) = \mathrm{V}_{\mathrm{x}} \qquad (2.21)$$

$$\mathrm{V}\,(\mathrm{M}_{\mathrm{x.c}}) + \mathrm{M}\,(\mathrm{V}_{\mathrm{x.c}}) = \mathrm{V}_{\mathrm{x}} \qquad (2.22)$$

$$\mathrm{V}\,(\mathrm{M}_{\mathrm{x.n}}) + \mathrm{M}\,(\mathrm{V}_{\mathrm{x.n}}) = \mathrm{V}_{\mathrm{x}} \qquad (2.23)$$

$$\mathrm{V}\,(\mathrm{M}_{\mathrm{x.rc}}) + \mathrm{M}\,(\mathrm{V}_{\mathrm{x.rc}}) = \mathrm{V}_{\mathrm{x}} \qquad (2.24)$$

Similarly we may derive and write without ambiguity, the two following identities:

$$V(M_{x.cn}) + M(V_{x.cn}) = V_x = V(M_{x.rn}) + M(V_{x.rn})$$

We shall later use a parameter V_{zn} which we define as:

$$\begin{aligned} V_x - V(M_{x.r}) - V(M_{x.c}) - M(V_{x.rc}) &= V_{zn} \\ = M(V_{x.r}) + M(V_{x.c}) - M(V_{x.cr}) - V_x & \qquad (2.25) \end{aligned}$$

By recourse to the operations defined already, we may also express V_{zn} alternatively as

$$V_{zn} = E(M_{x.rc} - M_{x.r} - M_{x.c} + M_x)^2.$$

For rapid computation, we define the following score totals and their squares:

$$T = \sum_{h=1}^{h=n} \sum_{i=1}^{i=c} \sum_{j=1}^{j=r} x_{hij} \; ; \; T_{ij} = \sum_{h=1}^{h=n} x_{hij} \; ; \; T_i = \sum_{h=1}^{h=n} \sum_{j=1}^{j=r} x_{hij}$$

$$T_j = \sum_{h=1}^{h=n} \sum_{i=1}^{i=c} x_{hij}$$

$$ncr.S = T^2 \; ; \; S_q = \sum_{h=1}^{h=n} \sum_{i=1}^{i=c} \sum_{j=1}^{j=r} x_{hij}^2$$

$$n.S_{cr} = \sum_{i=1}^{i=c} \sum_{j=1}^{j=r} T_{ij}^2 \; ; \; nr.S_c = \sum_{i=1}^{i=c} T_i^2 \; ; \; nc.S_r = \sum_{j=1}^{j=r} T_j^2$$

We may then write:

$$ncr.V_x = S_q - S \qquad (2.26)$$

$$ncr.V(M_{x.c}) = S_c - S \qquad (2.27)$$

$$ncr.V(M_{x.r}) = S_r - S \qquad (2.28)$$

$$ncr.M(V_{x.cr}) = S_q - S_{cr} \qquad (2.29)$$

$$ncr.V_{zn} = S + S_{cr} - S_c - S_r \qquad (2.30)$$

3. The sample distribution model.

It is implicit in the build-up of the random distribution of the *r*-fold sample by successive application of the chessboard device (fig. 2) that the distribution of individual scores in the entire assemblage of samples is that of the unit sample distribution, i. e. that of the parent universe, with mean M and variance V_u. The variance of the distribution of the *r*-fold score-sum being that of r independent unit samples is $(V_u + V_u + V_u \ldots) = r.V_u$, whence by appropriate scalar change that of the distribution of the mean sample score (M_s) is given by

$$\mathrm{V}(\mathrm{M_s}) = \frac{\mathrm{V_u}}{\mathrm{u}} \tag{3.1}$$

Now we may envisage each of the s samples of the chessboard lay-out as an array of r unit sample scores in a particular order, such arrays being disposable as a grid of s rows and r columns. With respect to such a grid we may denote by E_r and E_s respectively the operations of extracting the within-sample mean and the sample-to-sample mean of a score or parameter in accordance with the conventions of (2) above. In this notation we write the variance of the individual (fig. 2) score distribution within a particular sample as:

$$\sum_{\mathrm{i}=1}^{\mathrm{i}=\mathrm{r}} \frac{(\mathrm{x_i} - \mathrm{M_s})^2}{\mathrm{r}} = \mathrm{V_s} = \mathrm{E_r}(\mathrm{x_r^2}) - \mathrm{M_s^2} \tag{3.2}$$

The expected value of V_s in the sample-grid is then:

$$\mathrm{M}(\mathrm{V_s}) = \mathrm{E_s}.\mathrm{E_r}(\mathrm{x_r^2}) - \mathrm{E_s}(\mathrm{M_s^2}) \tag{3.3}$$

The total variance of the grid being that of the unit sample distribution, we may write

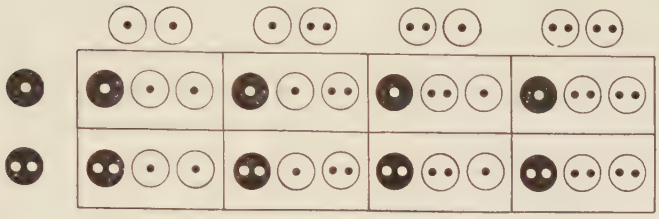
$$\mathrm{V_u} = \mathrm{E_s}.\mathrm{E_r}(\mathrm{x_r^2}) - \mathrm{M^2} \tag{3.4}$$

In the same notation:

$$\mathrm{V}(\mathrm{M_s}) = \mathrm{E_s}(\mathrm{M_s^2}) - \mathrm{M^2} = \frac{\mathrm{V_u}}{\mathrm{r}} \tag{3.5}$$

When we derive the familiar expression for the unbiassed estimate of the universe variance in conformity with the fundamental tautology of the grid:

THE UNBIASSED ESTIMATE OF VARIANCE



	MEAN (M_s)	M_s^2	$E_r(x_r^2) = \frac{1}{3}\sum x^2$	$V_s = \frac{1}{3}\sum x^2 - M_s^2$	$s^2 = \frac{3}{3-1} V_s$
⊙⊙ ⊙	$\frac{3}{3}$	$\frac{9}{9}$	$\frac{1}{3}(1^2+1^2+1^2) = 1$	$1 - \frac{9}{9} = 0$	0
⊙⊙ ⊙⊙	$\frac{4}{3}$	$\frac{16}{9}$	$\frac{1}{3}(1^2+1^2+2^2) = 2$	$2 - \frac{16}{9} = \frac{2}{9}$	$\frac{1}{3}$
⊙⊙ ⊙⊙	$\frac{4}{3}$	$\frac{16}{9}$	$\frac{1}{3}(1^2+2^2+1^2) = 2$	$2 - \frac{16}{9} = \frac{2}{9}$	$\frac{1}{3}$
⊙⊙ ⊙⊙	$\frac{5}{3}$	$\frac{25}{9}$	$\frac{1}{3}(1^2+2^2+2^2) = 3$	$3 - \frac{25}{9} = \frac{2}{9}$	$\frac{1}{3}$
⊙⊙ ⊙⊙	$\frac{4}{3}$	$\frac{16}{9}$	$\frac{1}{3}(2^2+1^2+1^2) = 2$	$2 - \frac{16}{9} = \frac{2}{9}$	$\frac{1}{3}$
⊙⊙ ⊙⊙	$\frac{5}{3}$	$\frac{25}{9}$	$\frac{1}{3}(2^2+1^2+2^2) = 3$	$3 - \frac{25}{9} = \frac{2}{9}$	$\frac{1}{3}$
⊙⊙ ⊙⊙	$\frac{5}{3}$	$\frac{25}{9}$	$\frac{1}{3}(2^2+2^2+1^2) = 3$	$3 - \frac{25}{9} = \frac{2}{9}$	$\frac{1}{3}$
⊙⊙ ⊙⊙	$\frac{6}{3}$	$\frac{36}{9}$	$\frac{1}{3}(2^2+2^2+2^2) = 4$	$4 - \frac{36}{9} = 0$	0
TOTAL:	$\frac{36}{3}$	$\frac{168}{9}$	20	$\frac{12}{9}$	2
MEAN, $E_s(\cdot\cdot)$:	$\frac{3}{2}$	$\frac{7}{3}$	$\frac{5}{2}$	$\frac{1}{6}$	$\frac{1}{4}$
	$M = E_s(M_s)$	$E_s(M_s^2)$	$E_s E_r(x_r^2)$	$M(V_s)$	$E_s(s^2)$

Variance of Unit Sample Distribution:
$V = (\frac{1}{2}+\frac{1}{2})^1 = \frac{1}{4} = \frac{5}{2} - (\frac{3}{2})^2$

Variance of Mean of 3-fold Samples:
$V(M_s) = \frac{7}{3} - (\frac{3}{2})^2 = \frac{1}{12} = \frac{V}{3}$

Mean of Variance of 3-fold Sample Score Distribution: $M(V_s) = \frac{1}{6}$

$M(V_s) = \frac{1}{6} = \frac{1}{4} - \frac{1}{12} = V - V(M_s)$
$\frac{3}{3-1} M(V_s) = \frac{1}{4} = V = E_s(s^2)$

Fig. 2. The Unbiassed Estimate of the Sample Variance. Visualisation of score-grid for 3-fold random samples of the toss of a flat circular die with one pip on one face and two pips on the other—one criterion of classification.

$$M(V_s) = V_u - V(M_s) = V_u - \frac{V_u}{r}$$

$$\therefore E_s(V_s) = \frac{r-1}{r} V_u \qquad (3.6)$$

Accordingly, we define a statistic whose expected value is V_u by the relations

$$E_s(s^2) = V_u \quad \textit{and} \quad s^2 = \frac{r}{r-1} V_s = \sum_{i=1}^{i=r} \frac{(x_i - M_s)^2}{r-1} \qquad (3.7)$$

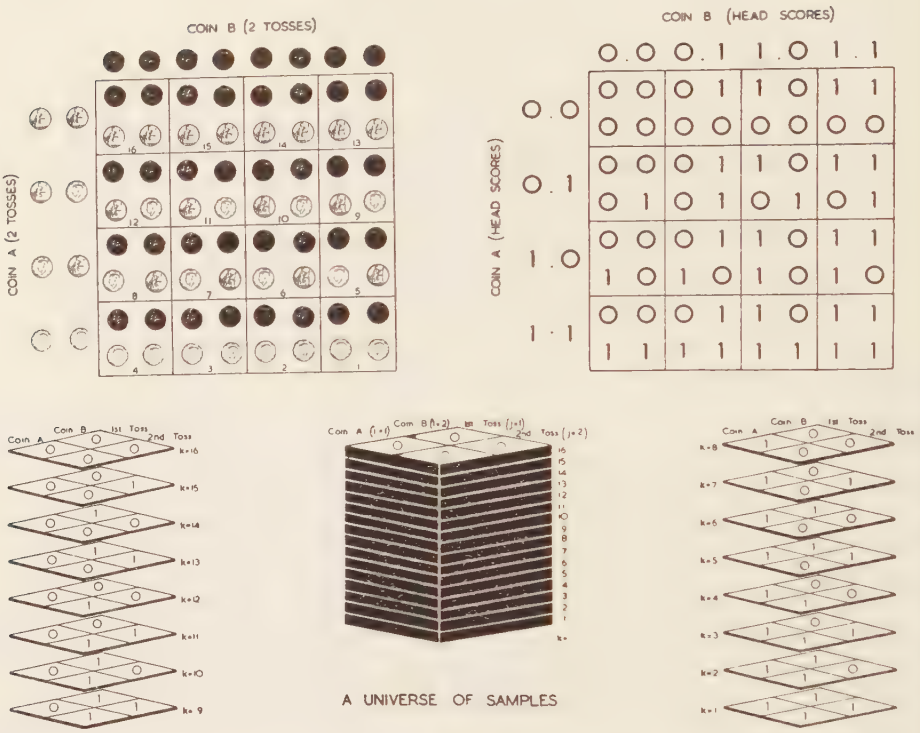


Fig. 3. The Homogeneous Universe of the Random Sample. Distribution of the 2-fold toss of each of two unbiassed coins—two criteria of classification.

The foregoing grid representation of the sample distribution involves only one criterion of sample structure, *viz.* identical toss-order of the same die. The *r*-fold toss of *c* identical unbiassed dice permits us to envisage a 2-way criterion of sample structure in terms of the identity of the dice and identical unit score sequence. Fig. 3, which shows the results of the 2-fold toss of each of 2 pennies exhibits the chessboard set-up for the derivation of the random sample distribution and the distribution itself as a 3-dimensional grid of *s* (= 16) layers corresponding to the *s* entries in the cells of the chess-board lay-out, Such is our model of a universe which is homogeneous with respect to 2 criteria of sample classification. Each layer is a sample of a particular structure with respect to row and column disposition of unit scores, and the distribution of unit-scores in the grid is necessarily that of the parent universe.

The distribution of scores in each pillar of the grid is that of a single trial, i. e. of a unit sample. To say that such a grid is homogeneous with respect to both criteria thus means that the distribution of individual scores within pillars, within row-slabs and within column-slabs alike is identical with the distribution of individual scores in the parent universe. If one die has a bias (fig. 4a and b) the universe will not be homogeneous with respect to one criterion of classification, i. e. if scores of the same column are referable to the same die, score distributions within pillars of the same column will be identical but not within the same row. Contrariwise, the score distributions of column slabs will not be identical, but that of row-slabs as a whole will be identical with that of the complete grid.

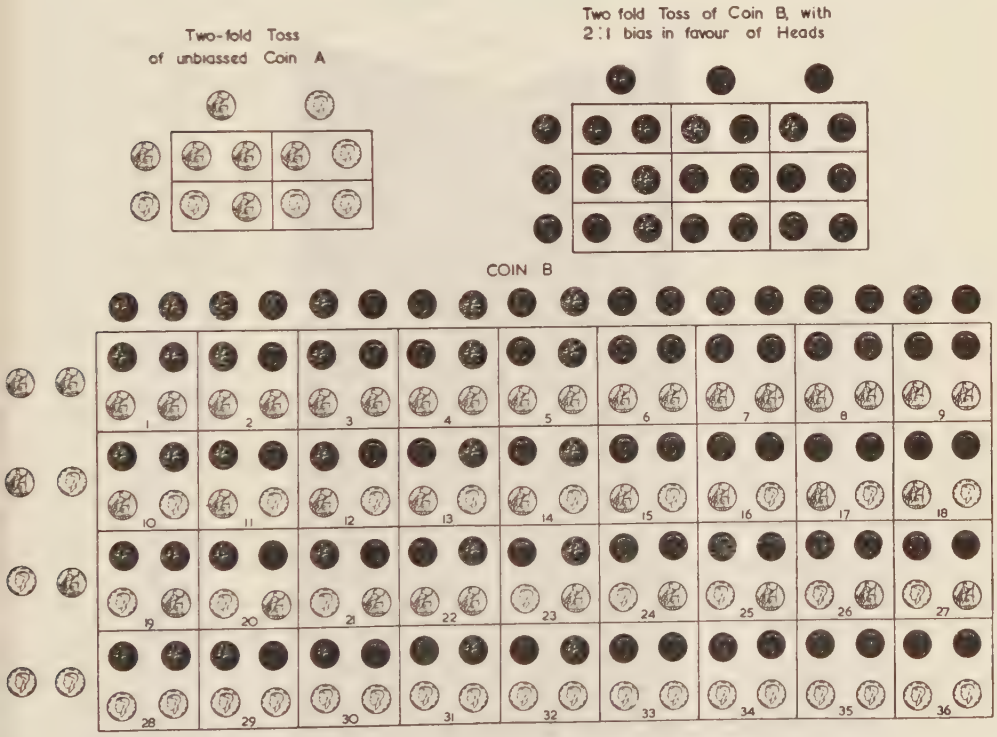


Fig. 4a. Chessboard derivation of the Random Sample Distribution of the 2-fold toss of two coins, one unbiassed, the other with a 2 : 1 bias in favour of heads.

These considerations suffice to clarify the conception of homogeneity with respect to one or both criteria of a structure in a random

system of samples classified in virtue of 2 alone. Though the major issue involved in this context involves such a dichotomy, it will be necessary for us to examine the implications of a classification involving *replication* as a third criterion. It is then still possible to visualise the complete distribution of a universe of random samples, if we represent each sample (fig. 5) as a 3-dimensional grid of n layers of rc scores. We thus conceive each sample as a stratum in a

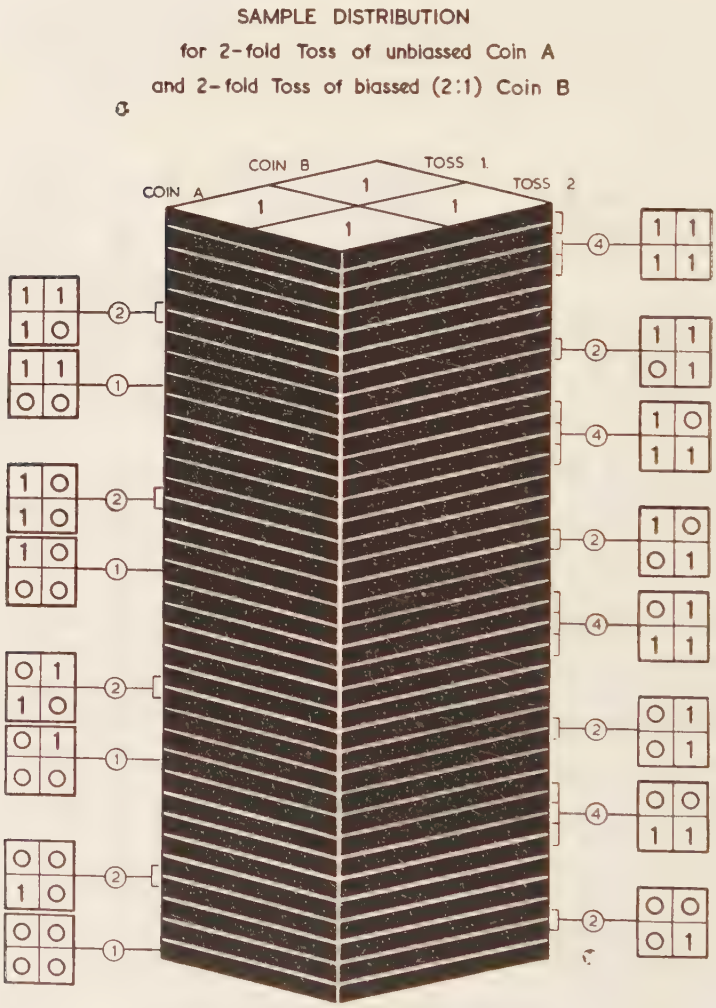


Fig. 4b. The Stratified 3-dimensional Universe of the Random Sample Distribution of fig. 4a.

universe grid of s strata. If y_k is the theoretical random frequency of a sample of particular structure, the number (f_s) of strata of corresponding structure is given by $sy_k = f_k$, and we define the operation of extracting the mean sample-to-sample value as for 2 criteria of classification by:

$$\frac{1}{s} \sum_{k=1}^{k=s} (u_k) = E_s (u_s) = \sum_{k=1}^{k=s} y_k . u_k \tag{3.8}$$

If we conceive the sample distribution as a continuum, we must replace the finite summation by an integral; but this does not affect the ensuing argument. The corresponding operation for extracting the mean of the n cells of a stratum-pillar or layers of a stratum, we define as before, *viz:*

$$\frac{1}{n} \sum_{h=1}^{h=n} (u_h) = E_n (u_n) \tag{3.9}$$

4. Criteria of homogeneity.

One class of procedures subsumed under the term *Analysis of Variance* has as its aim to decide whether a system of scores is homogeneous with respect to one or more criteria of classification, i. e. to test the null hypothesis that one or other putative source of variation implicit in the classificatory set-up is negligible. Our problem is then 2-fold:

(a) to define consistent relations between parameters of the score distribution referable to different dimensions of the sample grid and to the grid as a whole;

(b) to devise tests of the consistency of such parameters in accordance with what we may legitimately assume about the distribution of scores in the parent universe.

What we may legitimately or plausibly assume under (b) must depend on the situation, but we can define criteria of homogeneity implicit in (a) without invoking such additional postulates and without invoking other postulates requisite to the rationale of a balance sheet of variation. With this end in view we conceive our universe as in § 3 above.

If our concern is with only 2 criteria of classification, we shall denote a score of the cell in column c, row r and any layer (sample)

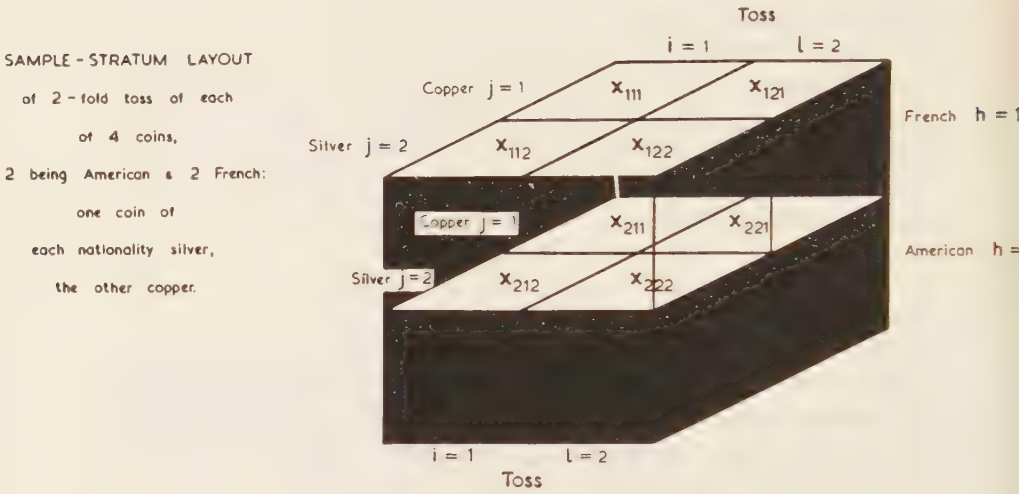


Fig. 5. The 3-dimensional grid of sample structure with respect to 3 criteria of classification.

k of the universe by x_{ijk}. When referable to a particular sample, we shall denote it as $x_{ij.s}$. Accordingly, we also distinguish the following sample parameters:

	No. of cells involved	Mean	Variance within
Row	c	$M_{x.rs}$	$V_{x.rs}$
Column	r	$M_{x.cs}$	$V_{x.cs}$
Sample (layer)	cr	$M_{x.s}$	$V_{x.s}$

For the true variance of the putatively homogeneous universe we may write $V_x = \sigma^2$. The evaluation of unbiassed estimates of σ^2 is simple in the notation of § 2 above, if we recall the fact we can perform the operations E_r, E_c and E_s over the grid as a whole in any order, so that

$$E_s.E_r\,(V_{x.rs}) = E_s.M\,(V_{x.rs}) = E_r.E_s\,(V_{x.rs}) \tag{4.1}$$

$$E_s.E_c\,(V_{x.cs}) = E_s.M\,(V_{x.cs}) = E_c.E_s\,(V_{x.cs}) \tag{4.2}$$

Since $V_{x.s}$, $V_{x.rs}$ and $V_{x.cs}$ are respectively referable to samples of rc of c and of r scores, by (3. 6) we have

$$E_s\,(V_{x.s}) = \frac{rc-1}{rc}\,\sigma^2\ ;\ E_s\,(V_{x.rs}) = \frac{c-1}{c}\,\sigma^2\ ;\ E_s\,(V_{x.cs}) = \frac{r-1}{r}\,\sigma^2 \tag{4.3}$$

Whence from (4.1) and (4.2) since these expressions are constants of the grid:

$$E_s.M\,(V_{x.rs}) = \frac{c-1}{c}\,\sigma^2 \quad \textit{and} \quad E_s.M\,(V_{x.cs}) = \frac{r-1}{r}\,\sigma^2 \tag{4.4}$$

If we now define $V_{z.s}$ in accordance with (2. 9):

$$E_s\,(V_{z.s}) = E_s.M\,(V_{x.rs}) + E_s.M\,(V_{x.cs}) - E_s\,(V_{x.s})$$

$$= \frac{c-1}{c}\,\sigma^2 + \frac{r-1}{r}\,\sigma^2 - \frac{rc-1}{rc}\,\sigma^2$$

$$\therefore\ E\,(V_{z.s}) = \frac{(r-1)\,(c-1)}{rc}\,\sigma^2 \tag{4.5}$$

Similarly, we have

$$E_s.V\,(M_{x.rs}) = E_s\,(V_{x.s}) - E_s.M\,(V_{x.rs}) = \frac{rc-1}{rc}\,\sigma^2 - \frac{c-1}{c}\,\sigma^2$$

$$\therefore\ E_s.V\,(M_{x.rs}) = \frac{r-1}{rc}\,\sigma^2 \tag{4.6}$$

$$E_s.V\,(M_{x.cs}) = E_s\,(V_{x.s}) - E_s.M\,(V_{x.cs}) = \frac{rc-1}{rc}\,\sigma^2 - \frac{r-1}{r}\,\sigma^2$$

$$\therefore\ E_s.V\,(M_{x.cs}) = \frac{c-1}{rc}\,\sigma^2 \tag{4.7}$$

We have now three statistics from which we can obtain unbiassed estimates of σ^2, and hence three statistics whose expected values must be consistent if the universe is homogeneous. One of these involves the variance of the row means only, one of the column means only, the other of both in accordance with 2. 10. From (4. 5)

$$E_s\,(s_z^2) = \sigma^2 \quad \textit{if} \quad s_z^2 = \frac{rc}{(r-1)\,(c-1)}\,V_{z.s} \tag{4.8}$$

For purposes of computation in the symbolism of (2. 15)

$$s_z^2 = \frac{S_q + S - S_c - S_r}{(r-1)\,(c-1)}\,. \tag{4.9}$$

From (4.6) we obtain:

$$E_s\,(c.s_r^2) = \sigma^2 \quad \textit{if} \quad s_r^2 = \frac{r}{r-1}\,V\,(M_{x.rs}) \tag{4.10}$$

Whence in the symbolism of (2.14):

$$c.s_r^2 = \frac{S_r - S}{r - 1} \tag{4.11}$$

From (4. 7) and (2. 13) we obtain:

$$E_s(r.s_c^2) = \sigma^2 \quad \textit{if} \quad s_c^2 = \frac{c}{c-1} V(M_{x.cs}) \tag{4.12}$$

$$r.s_c^2 = \frac{S_c - S}{c - 1} \tag{4.13}$$

Hence we arrive at the familiar table exhibiting unbiassed estimates of σ^2:

Square Totals from (2.12)–(2.15)	Divisor	Quotient	Expected Value
$S_r - S$	$r - 1$	$c.s_r^2$	σ^2
$S_c - S$	$c - 1$	$r.s_c^2$	σ^2
$S_q + S - S_c - S_r$	$(r - 1)(c - 1)$	s_z^2	σ^2
$S_q - S$	$rc - 1$	s^2	σ^2

In what follows our concern with the 3-way system arises only in connexion with *replication*. For reasons which will subsequently appear, we wish to establish that variation within the pillar of the sample stratum is wholly residual. Hence we seek to express σ^2 in terms of the expected values of sums of square deviations from the pillar means and of a statistic which takes into account variation in all three dimensions. In any case, we must accordingly refine our symbolism to take account of the new dimension of classification, as below:

	No. of cells	Mean Value of Variance within
Whole stratum	ncr	$E_s(V_{x.s}) = \frac{ncr - 1}{ncr}\sigma^2$
Row-slab	nc	$E_s(V_{x.rs}) = \frac{nc - 1}{nc}\sigma^2$
Column-slab	nr	$E_s(V_{x.cs}) = \frac{nr - 1}{nr}\sigma^2$
Pillar	n	$E_s(V_{x.rcs}) = \frac{n - 1}{n}\sigma^2$

The expected value of the mean square deviation of the score from the pillar mean, i. e. from the mean of scores referable to the same row and column classes is

$$E_s.M\,(V_{x.rcs}) = E_s.E_c.E_s\,(V_{x.rcs}) = \frac{n-1}{n}\sigma^2 \qquad (4.14)$$

Whence we define a statistic independent of sources of variation peculiar to the row, to the column or to the pillar criterion as:

$$E_s\,(s^2_{cr}) = \sigma^2 \quad \textit{if} \quad s^2_{cr} = \frac{n}{(n-1)}\,M\,(V_{x.rcs}) \qquad (4.15)$$

Whence by definition we may write:

$$s^2_{cr} = \frac{S\,(x_{hij} - M_{ij})^2}{(n-1)\,cr} \qquad (4.16)$$

In accordance with (2. 22) we may also define a statistic which takes into account variation from pillar to pillar as well as variation within the pillar, *viz :*

$$V_{zn.s} = M\,(V_{x.cs}) + M\,(V_{x.rs}) - M\,(V_{x.rcs}) - M\,(V_{x.s})$$

Whence from the code above:

$$E_s\,(V_{zn.s}) = \left(\frac{nr-1}{nr} + \frac{nc-1}{nc} - \frac{n-1}{n} - \frac{ncr-1}{ncr}\right)\sigma^2$$

$$\therefore\ E_s\,(V_{zn.s}) = \frac{(r-1)\,(c-1)}{ncr}\,\sigma^2$$

We may thus define the statistic s^2_{zn} by the relations

$$E\,(s^2_{zn}) = \sigma^2 \quad \textit{if} \quad s^2_{zn} = \frac{ncr}{(r-1)\,(c-1)}\,V_{zn.s} \qquad (4.17)$$

Whence in accordance with (2. 29) and (2. 30) for rapid computation:

$$s^2_{cr} = \frac{S_q - S_{cr}}{rc\,(n-1)} \qquad (4.18)$$

$$s^2_{zn} = \frac{S_{cr} + S - S_c - S_r}{(r-1)\,(c-1)} \qquad (4.19)$$

A criterion of homogeneity with respect to the replication criterion, i. e. absence of any source of variation peculiar to the pillar scores, will thus be the consistency of s^2_{cr} and s^2_{zn} defined by (4.18) and (4.19).

5. The balance sheet for two criteria.

The rationale of significance tests designed to assess the consistency of estimates specified in the foregoing section is irrelevant to the issue under discussion. It will suffice to assume that we are entitled to make appropriate formal assumptions additional to those so far invoked, and that the outcome of the performance of a significance test is to encourage the belief that agencies associated with the several dimensions of classification contribute significantly to variation within the sample. One may then ask how much variation arises from one or other source. In this context, our measure of variation is variance; and it is pertinent to remark that our choice of such a measure depends less on any unique claims to consideration from a semantic viewpoint than on the mathematical convenience of its properties.

Nothing said so far implies the possibility of undertaking what analysis of variance connotes in the most literal sense of the term as stated above, i. e. to estimate what fractions of total variance in the universe of sampling are respectively attributable to agencies associated with the several criteria of classification employed or to residual sources. The credentials of any such balance sheet depend on a new set of assumptions, which we may specify under three headings:

(a) *causal*, inasmuch as they prescribe how the several sources of variation respectively contribute to a particular score value:

(b) *statistical*, inasmuch as they refer to the distribution of the score components singly or jointly;

(c) *operational*, inasmuch as they depend on the prospective use of information supplied by the sample.

To clarify this threefold distinction, it will be helpful to cite a model experiment in which nature and nurture appear as the two criteria of classification. On six consecutive occasions with a 4-hour interval between any one and its predecessor or successor, a laboratory worker makes one determination of the blood calcium level of each of five rabbits, using the same five throughout. If we set out the 30 observations (scores) in a 5 (columns) by 6 (rows) table, we have to deal with three putative sources of variation:

(i) a rhythm of variation within the 24 hour period in one and the same animal, its effect being therefore such as to increase variation between the row means;

(ii) systematic differences of the absolute level between animals at one and the same time, their effect being such as to increase variation in the column means;

(iii) random errors of measurement sufficient to ensure cell to cell variation in the absence of either of the systematic components, and hence also some variation in row and column means.

It is admissible to conceive the possibility that each cell score in this set-up has three strictly additive components, which we shall refer to respectively as the residual, the column factor and the row factor. This constitutes a *causal* assumption. *Ex hypothesi*, the row factor varies from row to row, being constant from column to column and the column factor varies from column to column being constant from row to row within the sample; but we are free to postulate random distribution of the residual from cell to cell in each dimension of the grid. This is a *statistical* assumption, as is the postulate that there is *zero covariance* between the three components.

Neither the assumption of additivity nor that of zero covariance is necessarily true of any particular situation. They are attractive from a statistical viewpoint, because *the variance of the distribution of the sum of n variates is the sum of the variance of each, if the covariances are zero.* This circumstance makes it possible to express the total variance of a system as a sum of additive components; and that indeed is what we mean when we speak of a balance sheet of variance.

Having adopted these postulates with more or less plausibility we are not yet in a position to proceed. For we have still to make an *operational* assumption, without which no unique solution is possible. Until we have decided within what framework of reference we choose to regard our experiment as a random sample, we are not in a position to undertake our analysis. In effect, this signifies that we have to find an answer to the question: in what way do we propose to repeat the experiment? One may repeat the experiment last cited in four ways:

(i) by making n different determinations on each animal at one and the same time;

(ii) by making observations at corresponding times in the course of the 24-hour period on the same set of rabbits on successive days;

(iii) by making corresponding observations on more than one set of rabbits on one and the same day;

(iv) by making corresponding observations on different sets of rabbits on successive days.

Evidently, the only use of an exhaustive balance sheet exhibiting components of variance is to prescribe what is likely to happen, if one does the same thing again. Evidently also, the sources of variation are not the same in the four ways which one might choose to regard as doing the same thing again in this context. The first implies that row and column factors remain constant throughout. The second and third respectively imply that the column factor alone or the row factor alone vary from one trial to another. The last signifies that both row and column factors vary, and leaves us free to postulate that they vary from sample to sample at random; hence also to invoke with more or less propriety a distribution law consonant with the possibility of assigning confidence limits to the entries of our balance sheet.

On this account, *Churchill Eisenhart* (*op. cit.*), who distinguishes between (i) and (iv) above as *Model I* and *Model II* situations, emphasises the distinction between them with particular reference to: (a) precautions taken to ensure random sampling in the design of the experiment; (b) whether the end in view is merely to assess the role of error variance or to effect a complete partition of the components of variation. *Lee Crump* (1946), on the other hand, is more explicit about what we here regard to be the focal issue, *viz.* the operational intention.

The following assumptions are common to the treatment of the problem in accordance with the postulates of either Model I or Model II:

(i) Three strictly additive components contribute to the sample cell-score $x_{ij.s}$ in accordance with the following equation in which $e_{ij.s}$ is the residual, $F_{i.cs}$ the column factor and $F_{j.rs}$ the row factor:

$$x_{ij.s} = e_{ij.s} + F_{i.cs} + F_{j.rs} \qquad (5.1a)$$

(ii) The covariance of any pair of components is zero, i. e.

$$Cov\,(e_{ijk}, F_{ik.c}) = Cov\,(e_{ijk}, F_{jk.r}) = Cov\,(F_{ik.c}, F_{jk.r}) = 0 \qquad (5.1b)$$

(iii) If $\sigma^2 = V_x$ is the variance of the total score x_{ijk} in the universe, and σ^2_e, σ^2_c, σ^2_r are the corresponding variances of the score components in (5. 1a), it follows that:

$$\sigma^2 = \sigma^2_e + \sigma^2_c + \sigma^2_r \qquad (5.1c)$$

(iv) The residual component e_{ijk} varies from cell to cell within the row and within the column of the sample random-wise, so that the distribution of residual score components is the same in all pillars of the 3-dimensional grid of the complete random sample distribution.

$x_{11s} = \epsilon_{11s}$	$x_{21s} = \epsilon_{21s}$	$x_{31s} = \epsilon_{31s}$
$x_{12s} = \epsilon_{12s}$	$x_{22s} = \epsilon_{22s}$	$x_{32s} = \epsilon_{32s}$
$x_{13s} = \epsilon_{13s}$	$x_{23s} = \epsilon_{23s}$	$x_{33s} = \epsilon_{33s}$

HOMOGENEOUS CASE

Column Factor		F_{1c}	F_{2c}	F_{3c}
	Column (i):	i = 1	i = 2	i = 3
Row (j)				
j = 1		$\epsilon_{11s} + F_{1c} + F_{1r}$	$\epsilon_{21s} + F_{2c} + F_{1r}$	$\epsilon_{31s} + F_{3c} + F_{1r}$
j = 2		$\epsilon_{12s} + F_{1c} + F_{2r}$	$\epsilon_{22s} + F_{2c} + F_{2r}$	$\epsilon_{32s} + F_{3c} + F_{2r}$
j = 3		$\epsilon_{13s} + F_{1c} + F_{3r}$	$\epsilon_{23s} + F_{2c} + F_{3r}$	$\epsilon_{33s} + F_{3c} + F_{3r}$

MODEL I

Column Factor $F_{i.cs}$ constant within column of sample (layer) and within column-slab of universe (3-dimensional grid)

Row Factor $F_{j.rs}$ constant within row of sample (layer) and within row-slab of universe (3-dimensional grid)

Row Factor	Column Factor:	$F_{1.cs}$	$F_{2.cs}$	$F_{3.cs}$
	Column (i):	i = 1	i = 2	i = 3
	Row (j)			
$F_{1.rs}$	j = 1	$\epsilon_{11s} + F_{1.cs} + F_{1.rs}$	$\epsilon_{21s} + F_{2.cs} + F_{1.rs}$	$\epsilon_{31s} + F_{3.cs} + F_{1.rs}$
$F_{2.rs}$	j = 2	$\epsilon_{12s} + F_{1.cs} + F_{2.rs}$	$\epsilon_{22s} + F_{2.cs} + F_{2.rs}$	$\epsilon_{32s} + F_{3.cs} + F_{2.rs}$
$F_{3.rs}$	j = 3	$\epsilon_{13s} + F_{1.cs} + F_{3.rs}$	$\epsilon_{23s} + F_{2.cs} + F_{3.rs}$	$\epsilon_{33s} + F_{3.cs} + F_{3.rs}$

MODEL II.

Column Factor $F_{i.cs}$ constant within column of sample (layer) variable within column-slab of universe (3-dimensional grid) row-slab and column-slab distributions identical with one another and with that of whole grid

Row-Factor $F_{j.rs}$ constant within row of sample (layer) variable within row-slab of universe (3-dimensional grid) column-slab and row-slab distributions identical with one another and with that of whole grid

Fig. 6a. Sample Structure for 2 criteria of classification in accordance with Model I and Model II of Churchill Eisenhart (*see text*).

(v) Within the same layer of the 3-dimensional grid, $F_{i.cs}$ varies from cell to cell *only* within the row, being fixed for the column, and $F_{j.r}^{s}$ varies from cell to cell *only* within the column, being fixed within the row.

(vi) Accordingly, the distribution of the column factor in the sample as a whole is identical with its row distribution, all rows being alike with reference thereto; and the distribution of the row factor in the sample as a whole is identical with its column distribution, all columns being in this respect alike.

The foregoing assumptions are common to both Models. The postulates peculiar to Model I are:

(vii) $F_{i.cs}$ is fixed for all cells within the same column slab as well as for all cells within the same column of the same layer, and $F_{j.rs}$ is fixed for all cells within the same row-slab as well as for all cells of the same row within the same layer.

(viii) Hence the variance of the row factors within a column as within a layer is σ_r^2 and the variance of the column factors within a row as within a layer is σ_c^2.

Contrariwise, the postulates of Model II will be that $F_{i.cs}$ and $F_{j.rs}$ vary at random from layer to layer in the sense that:

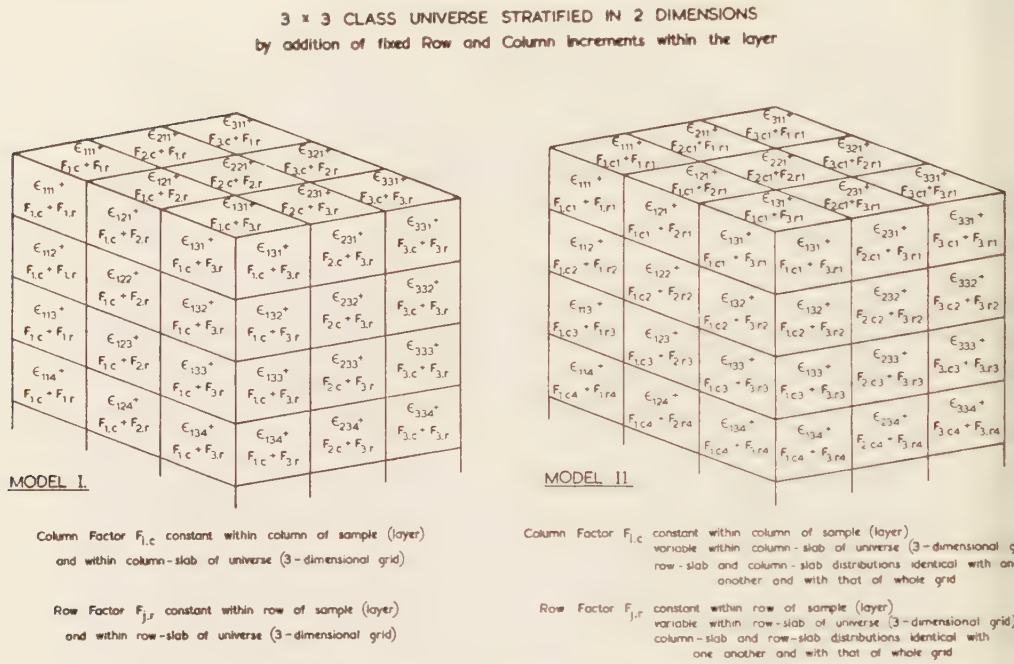


Fig. 6b. The Stratified Universe of Models I and II in 6. A.

(ix) each row-slab and each pillar therein accommodates a complete random distribution of column factors identical with the distribution of column factors in the 3-dimensional grid as a whole, whence also in virtue of (v) and (vi) identical with the distribution of column factors in the column-slab.

(x) each column-slab and each pillar therein accommodates a complete random distribution of row-factors identical with the distribution of column factors in the whole 3-dimensional grid, whence likewise in virtue of (v) and (vi) identical with the row-slab distribution of row factors.

In what follows we shall first explore the consequences of the Model II postulates. The only new consideration of moment arising from the foregoing definitions is then that the whole *rc*-fold sample of *x*-scores supplying us with an *rc*-fold sample of *e*-scores is a *c*-fold sample of row factors on account of the identity of the rows with respect to the latter and an r-fold sample of column-factors on account of the identity of the columns with respect thereto. We may express this otherwise by saying that the sample as a whole furnishes us with no information about the column-factors other than what we may infer from the composition of any one of the

rows alone, and no information about the row-factors other than what we may infer from any one of the columns equally.

In accordance with Model II postulates, we shall need symbols for the variances of the score components as below:

	Residual	Row factor	Column factor
Whole sample (layer)	$V_{e.s}$	$V_{r.s} = V_{r.cs}$	$V_{c.s} = V_{c.rs}$
Within-row	$V_{e.rs}$	$V_{r.rs} = 0$	$V_{c.rs}$
Within-column	$V_{e.cs}$	$V_{r.cs}$	$V_{c.cs} = 0$

From what has been said, the expected values of the above are:

$$E_s(V_{e.s}) = \frac{rc-1}{rc}\sigma_e^2 \quad E_s(V_{r.s}) = \frac{r-1}{r}\sigma_r^2 \quad E_s(V_{c.s}) = \frac{c-1}{c}\sigma_c^2$$

$$E_s(V_{e.rs}) = \frac{c-1}{c}\sigma_e^2 \qquad 0 \qquad E_s(V_{c.rs}) = \frac{c-1}{c}\sigma_c^2$$

$$E_s(V_{e.cs}) = \frac{r-1}{r}\sigma_e^2 \quad E_s(V_{r.cs}) = \frac{r-1}{r}\sigma_r^2 \qquad 0$$

We now recall the procedure of which the following is a pattern:

$$E_s.M(V_{e.cs}) = E_s.E_c(V_{e.cs}) = E_c.E_s(V_{e.cs}) = \frac{c-1}{c}\sigma_e^2$$

If the components have zero covariance

$$V_{x.s} = V_{e.s} + V_{c.s} + V_{r.s}$$

$$V_{x.rs} = V_{e.rs} + V_{c.rs} \quad \textit{and} \quad V_{x.cs} = V_{e.cs} + V_{r.cs}$$

Whence we derive:

$$E_s(V_{x.s}) = \frac{rc-1}{rc}\sigma_e^2 + \frac{r-1}{r}\sigma_r^2 + \frac{c-1}{c}\sigma_c^2 \tag{5.2}$$

$$E_s.M(V_{x.rs}) = \frac{c-1}{c}\sigma_e^2 + \frac{c-1}{c}\sigma_c^2 \tag{5.3}$$

$$E_s.M(V_{x.cs}) = \frac{r-1}{r}\sigma_e^2 + \frac{r-1}{r}\sigma_r^2 \tag{5.4}$$

If V_s has the same meaning as in § 4.

$$E_s(V_z) = E_s.M(V_{x.rs}) + E_s.M(V_{x.cs}) - E_s(V_{x.s})$$
$$= \left(\frac{c-1}{c} + \frac{r-1}{r} - \frac{rc-1}{rc}\right)\sigma_e^2$$
$$E_s(V_z) = \frac{(r-1)\ (c-1)}{rc}\sigma_e^2$$

Accordingly, we may define a statistic by the relations:

$$E_s(s_z^2) = \sigma_e^2 \quad \textit{and} \quad s_z^2 = \frac{rc}{(r-1)\ (c-1)} V_z$$

For purposes of computation, (4.9) defines s_z^2 in the above. Similarly we have:

$$E_s.V(M_{x.cs}) = E_s(V_{x.s}) - E_s.M(V_{x.cs})$$
$$= \frac{rc-1}{rc}\sigma_e^2 + \frac{c-1}{c}\sigma_c^2 + \frac{r-1}{r}\sigma_r^2 - \frac{r-1}{r}\sigma_e^2 - \frac{r-1}{r}\sigma_r^2$$
$$= \frac{c-1}{rc}\sigma_e^2 + \frac{c-1}{c}\sigma_c^2$$

Accordingly, we define a statistic by the relations:

$$E_s(r.s_c^2) = \sigma_e^2 + r\sigma_c^2 \quad \textit{and} \quad s_c^2 = \frac{c}{c-1} V(M_{x.cs}) \qquad (5.6)$$

In the same way we derive the statistic defined by

$$E_s(c.s_r^2) = \sigma_e^2 + c\sigma_r^2 \quad \textit{and} \quad s_r^2 = \frac{r}{r-1} V(M_{x.rs}) \qquad (5.7)$$

For purposes of computation (4.11) and (4.13) respectively define s_r^2 and s_c^2.

We may thus set out the *Model II* balance sheet as follows:

Square Totals from (2. 12)–(2. 15)	Divisors	Expected Value
$S_c - S$	$r(c-1)$	$\frac{1}{r}\sigma_e^2 + \sigma_c^2$
$S_r - S$	$c(r-1)$	$\frac{1}{c}\sigma_e^2 + \sigma_r^2$
$S_q + S - S_c - S_r$	$(r-1)\ (c-1)$	σ_e^2

By eliminating σ_e^2 from the first two items we obtain:

Component	Unbiassed Estimate
σ_c^2	$\frac{S_c - S}{(r-1)(c-1)} - \frac{S_q - S_r}{r(r-1)(c-1)}$
σ_r^2	$\frac{S_r - S}{(r-1)(c-1)} - \frac{S_q - S_c}{c(r-1(c-1)}$
σ_e^2	$\frac{S_q + S - S_c - S_r}{(r-1)(c-1}$

Let us now examine the consequences of assuming that the column factor is constant from sample to sample, i. e.

$$E_s(V_{i.s}) = \sigma_c^2 = E_s(V_{i.rs})$$

We then obtain:

$$E_s(V_{x.s}) = \frac{rc-1}{rc}\sigma_e^2 + \frac{r-1}{r}\sigma_r^2 + \sigma_c^2$$

$$E_s(V_{x.cs}) = \frac{r-1}{r}\sigma_e^2 + \frac{r-1}{r}\sigma_r^2$$

$$E_s(V_{x.rs}) = \frac{c-1}{c}\sigma_e^2 + \sigma_c^2$$

This does not affect the derivation of the expected value (s_z^2) of V_z as defined by (5. 5), nor that of s_r^2 as defined by (5.7); but

$$E_s.V(M_{x.cs}) = \frac{rc-1}{rc}\sigma_e^2 + \frac{r-1}{r}\sigma_r^2 + \sigma_c^2 - \frac{r-1}{r}\sigma_e^2 - \frac{r-1}{r}\sigma_r^2$$

$$= \frac{c-1}{rc}\sigma_e^2 + \sigma_c^2$$

$$E_s(r.s_c^2) = \sigma_e^2 + \frac{rc}{c-1}\sigma_c^2 \qquad (5.8)$$

Similarly, it will not affect the meaning of s_z^2 or s_c^2 if we postulate that the row factor remains constant from sample to sample; but we then derive

$$E_s(c.s_r^2) = \sigma_e^2 + \frac{rc}{r-1}\sigma_r^2 \qquad (5.9)$$

If both systematic components remain fixed from sample to sample both (5.8) and (5.9) hold good; and our balance (Model I) sheet is as below:

Square Totals from (2. 12)–(2. 15)	Divisors	Expected Value
$S_c - S$	$r(c-1)$	$\frac{1}{r}\sigma_e^2 + \frac{c}{c-1}\sigma_c^2$
$S_r - S$	$c(r-1)$	$\frac{1}{c}\sigma_e^2 + \frac{r}{r-1}\sigma_r^2$
$S_q + S - S_c - S_r$	$(r-1)(c-1)$	σ_e^2

If we conceive the sample as an *n*-layered stratum, we can visualise the construction of a balance sheet of a set-up involving 3 criteria of classification on various assumptions of which only one is relevant to our purpose (*vide infra*), namely that: (a) there is a third strictly additive factor $F_{ij.s}$ constant within the pillar; (b) there is zero covariance between any pair of the three systematic factors and residual component; (c) the variation of $F_{ij.s}$ is random from one sample (stratum) to another. The requisite relations are then in Table IV, from which the items of the balance sheet of *Lee Crump* (1946) are deducible. The author last named examines the issue consistently through the spectacles of Model II. The schema of Table IV requires appropriate modification, if we adopt the Model I assumptions with respect to row and column factors; but we cannot derive an estimate of σ_{cr}^2 from the statistics s_{cr}^2 and s_{zn}^2 of §4 unless we make the assumption (c) above. Indeed, the components of variance specified by *Daniels* (1947) who looks at the problem through the spectacles of Model I are arbitary as he himself concedes.

6. *The additive principle.*

In seeking a rationale for the construction of a balance sheet of variation we have postulated a universe of scores with 3 components, a column factor, a row factor and a residual. On the assumption that there is zero covariance between any pair of them, the true variance of the composite score in the universe of choice is the sum of the variances of the three components, i. e. $\sigma^2 = \sigma_e^2 + \sigma_r^2 + \sigma_c^2$. Thus σ_e^2 stands for what the total variance would be if there were no source of systematic variation associated with the row and column criteria of classification. The tidiness of this relation has a deceptive air of finality. So it is important that the student should

Table IV.

Replication set-up involving row factors, column factors and a third factor variable from cell but fixed within pillar of sample stratum.

	Residual ($e_{hij.s}$)	*Row factor* ($F_{j.rs}$)	*Column factor* ($F_{i.cs}$)	*Cell factor* ($F_{ij.s}$)
whole stratum	$E_s.V_{e.s} = \frac{ncr-1}{ncr}\sigma_e^2$	$E_s.V_{r.s} = \frac{r-1}{r}\sigma_r^2$	$E_3.V_{c.s} = \frac{c-1}{c}\sigma_c^2$	$E_s.V_{n.s} = \frac{rc-1}{rc}\sigma_{cr}^2$
stratum	$E_s.V_{e.rs} = \frac{nc-1}{nc}\sigma_e^2$	$E_s.V_{r.rs} = 0$	$E_s.V_{r.rs} = \frac{c-1}{c}\sigma_c^2$	$E_s.V_{n.rs} = \frac{c-1}{c}\sigma_{cr}^2$
column stratum	$E_s.V_{e.cs} = \frac{nr-1}{nr}\sigma_e^2$	$E_s.V_{r.cs} = \frac{r-1}{r}\sigma_r^2$	0	$E_s.V_{n.cs} = \frac{r-1}{r}\sigma_{cr}^2$
pillar	$E_s.V_{e.rcs} = \frac{n-1}{n}\sigma_e^2$	0	0	0

understand what factual assumptions entitle us to construct a balance sheet in accordance with the algebraic postulates of § 5.

From the factual viewpoint, the pivotal postulate is that the row and column factors are *strictly additive*. This signifies that effects of sources of variation associated with the two class systems are such as to change the mean value of the row or column score distribution without changing its form or scale. Now it is easy to imagine many other ways in which variation might arise. In much experimental work, change of scale or dispersion without change of mean in virtue of the competence of the worker is just as likely an assumption, perhaps more so. Hence the attractiveness of the additive postulate resides less in its relevance to external nature than to the convenience of the mathematician. Of this, as of other assumptions commonly made in relation to the same class of procedures, we may cite the comment of *Churchill Eisenhart* (1946): "the only motivation that has been given is the more general nature of the inferences that may be drawn .... when it is satisfied."

In any real situation, it therefore behoves us to ask whether the additive postulate is indeed plausible; and it is conspicuously open to question in the field of earliest and most extensive applications of variance analysis. Here again the remarks of *Churchill Eisenhart* (*op. cit.*) are explicit and salutary:

> Hence, when additivity does not prevail we say that there are interactions between row and column factors. Thus, in the case of varieties and treatments .... additivity implies that, under the general experimental conditions of the test, the true mean yield of one variety is greater (or less) than the true mean yield of another

variety by an amount—an additive constant, not a multiplier—that is the same for each of the treatments concerned, and, conversely, the true mean yield with one treatment is greater (or less) than the true mean yield with another treatment by an amount which does not depend upon the variety concerned; which is exactly what is meant when we say that there are no "interactions" between varietal and treatment effects.

Mathematicians who are not conversant with the vagaries of gene exhibition and biologists who are not at home with the technical intricacies of the thesis expounded by the writer of the remarks cited above will not regard it as unprofitable to pinpoint what is of cardinal importance to the present discussion by reference to a naturalistic illustration. Our supposition is that we record in 3 different environments the size (*yield*) attained at a given age by individuals of two species of flowering plants, one (A) being calciphil and the other (B) being calciphobe. The three environments (*treatments*) being the native soil (untreated), native soil with addition of a neutral calcium salt and native soil treated with a neutral potassium salt. To drive home the point *Churchill Eisenhart* makes in his reference to treatment (*nurture*), variety (*nature*) and yield (*phenotype*), we may disregard the residual component of the cell score (*yield*) arising from random errors of measurement and uncontrolled subsidiary differences with respect to environment. If we denote the cell score in the absence of residual error so defined as u_{ij}, the column (*species*) factors respectively by F_a and F_b, and the row (*treatment*) factors as F_1, F_2 and F_3, our set-up as prescribed by the additive postulate is:

	Species A	Species B
Untreated (r = 1)	$u_{11} = (F_a + F_1)$	$u_{21} = (F_b + F_1)$
Excess Ca (r = 2)	$u_{12} = (F_a + F_2)$	$u_{22} = (F_b + F_2)$
Excess K (r = 3)	$u_{13} = (F_a + F_3)$	$u_{23} = (F_b + F_3)$

The implications of this become more obvious, if we set the result out thus:

	Species A	Species B
Effect of Ca	$(u_{12} - u_{11}) = (F_2 - F_1)$	$= (u_{22} - u_{21})$
Effect of K	$(u_{13} - u_{11}) = (F_3 - F_1)$	$= (u_{23} - u_{21})$

The above schema signifies that a fixed excess of *Ca* increases the size of B and A by an equal amount, a statement which is inconsistent with our own initial assumption that the two species are respectively calciphobe and calciphil Likewise the additive postulate signifies in this context that B and A react by equal responses to a fixed increment of K, an assertion inconsistent with general experience of ionic antagonisms in the biological domain. On the contrary, we should expect a calciphil species which reacts by increased yield to increase of *Ca* soil content to react by diminished yield to excess of *K*, and a calciphobe species which reacts by diminished yield to increase of the Ca soil content to react by increased yield to excess of K.

From the field of interspecific variation, it would be possible to cite numberless examples of comparable situations, but the writer has sufficiently emphasised their occurrence within the domain of intraspecific variation. More recently *Haldane* (1946) has classified known types of interaction, i. e. departure from the assumption of additivity, by recourse to experimental data. It is indeed open to question whether there exists any nature-nurture situation about which we can make any such assumptions with confidence in the absence of corroboration, or whether it will often happen that such an assumption is plausible. What is certain, as illustrated by the foregoing example, is likewise embodied in the adage that one man's meat is another man's poison. Many situations arise in which stimulus X increases response of genotype A and inhibits that of genotype B, while stimulus Y decreases response of genotype A and augments that of genotype B. If it is necessary to remind the biologist familiar with his materials that the additive postulate may therefore be grossly inapplicable to a set-up in which the two classificatory criteria are nature and nurture, it is because relatively few biologists who invoke the technique under discussion with a view to the construction of a balance sheet exhibiting the respective contributions of nature and nurture variables realise that the additive postulate is in fact the keystone of the entire edifice.

Accordingly, we may thus sum up the outcome of our enquiry at this stage:

(1) The possibility of constructing a true bill which sets out what fractions of total population variance are respectively attributable to one or other source of variation specified by the class criteria and

to residual errors of observation or other uncontrolled circumstances presupposes the truth of the postulate that the components are additive.

(2) From inspection of the data of a single small-scale experiment it is never possible to infer with certainty that this postulate is valid[1]), and there will arise many situations in which it is grossly incorrect.

These considerations prompt us to ask: is it possible to justify the additive postulate by recourse to observation, and if so, how? To answer this, we shall suppose that the joint contribution of $F_{i.cs}$ and $F_{j.rs}$ to the score value exceeds or falls short of their sum by an amount $F_{ij.s}$ which varies from cell to cell, i. e.:

$$x_{ij.s} = e_{ij.s} + F_{i.cs} + F_{j.rs} + F_{ij.s}$$

Evidently the expected value of s_z^2 in § 4 and § 5 will not be σ_e^2 unless $F_{ij.s} = 0$, and the design of an experiment involving single score values for each cell in a 2-way layout provides no occasion for distinguishing between two components which both vary from cell to cell. On the other hand, their effects are distinguishable if we resort to *n*-fold *replication*, i. e. *n*-fold repetition of each observation without changing the row and column sources of variation. In such an experimental design, we conceive our sample as a stratum of *n* layers. The residuals vary random-wise from cell to cell within a layer and from layer to layer within a pillar. If the replication is faithful, the component $F_{ij.s}$ varies from cell to cell within a layer but not within a pillar. Accordingly, we can ask whether the measures of cell-to-cell variation within a pillar (s_{cr}^2 in § 4 above) and within a stratum (s_{zn}^2) are consistent, i. e. if $F_{ij.s} = 0$, in a set-up for 3 criteria of classification involving replication as the new one.

The construction of a balance sheet for an experiment involving replication is valid only if: (a) the analysis fails to disclose a new component of variation; (b) we have other reasons for assuming that 3 systematic components conform to the postulates of additivity and zero covariance. If the results of identical replication do *not* confirm the assumption that the postulate is valid, the inclusion of a separate component of *interaction* as defined by *Churchill Eisenhart* in the balance sheet of causality merely serves to announce that *the procedure for constructing it is defective, hence also that it is not a true bill.*

[1]) *Tukey* (1949) discusses the possibility of inferring departure from additivity on certain special assumptions including that the discrepancy is in fact small.

If there is indeed good reason to believe that the additive principle holds good, we may then interpret our Balance Sheet as:

(i) a recipe for assigning to what errors mean measurements are subject when we exclude one or other source of variation;

(ii) an overall picture of how much variability remains when we eliminate one or other source.

To clarify the meaning of (i), the illustrative (p. 122) experiment already cited will serve our purpose. At a given time of day, the data supply us with a mean figure for the blood calcium level of different rabbits. This figure is therefore subject both to residual sampling error inherent in the method of measurement and to variation arising from the fact that different measurements refer to 5 different individuals. The unbiassed estimate of the residual variance being s_e^2, that of the mean of a 5-fold sample is $\frac{1}{5}(s_e^2)$ Alternatively, we may ask what would be the sampling variance for the mean of the series of 6 determinations on the same rabbit at different times of day or night, i. e. to what sampling variance our column means referable to the same rabbit are subject as the result of errors of measurement alone. In this case, our concern is with the mean of a 6-fold sample, and the required parameter is $\frac{1}{6}(s_e^2)$ In general, we may say that the mean row scores and the mean column scores are respectively subject to sampling variance of $(s_e^2 \div c)$ and $(s_e^2 \div r)$.

An alternative conception of the sort of questions an accredited Balance Sheet of Variance may answer brings into focus an important difference between *Model I* and *Model II* of § 5. As an assemblage of unbiassed estimates of universe components of variance, the balance sheet would appear to be just as valid, if constructed on one or other assumption; but we may wish to take the further step of placing fiducial limits around each of our estimates of the components. To do so, we must then invoke certain assumptions concerning the distribution of the row and column factors. If we scrutinise our experimental data through the spectacles of *Model II*, we are free to postulate with more or less justification a normal distribution of all three score components in the universe as a whole. Thereafter the problem stated is purely mathematical, if we are entitled to regard the choice of sample as random.

Writers on analysis of variance are not slow to stress the fact that random choice of column or row score components is often inconsistent with experimental design, as in the following remarks of *Churchill Eisenhart:*

"... . when an experimenter selects two or more treatments, or two or more varieties, for testing, he rarely, if ever, draws them at random from a population of possible treatments or varieties; he selects those that he believes are most promising. Accordingly Model I is generally appropriate where treatment, or variety comparisons are involved. On the other hand, when an experimenter selects a sample of animals from a herd or a species, for a study of the effects of various treatments, he can insure that they are a random sample from the herd, by introducing randomization into the sampling procedure, for example, by using a table of random numbers. But he may consider such a sample to be a random sample from the species, only by making the assumption that the herd itself is a random sample from the species. In such a case, if several herds (from the same species) are involved, Model II would clearly be appropriate with respect to the variation among the animals from each of the respective nerds, and might be appropriate with respect to the variation of the herds from one another."

Lee Crump (1946) writes in the same vein:

"*A Note of Warning.* It must be remembered that in using the analysis of variance to estimate variance components, we have assumed the elements of the fundamental equation to be randomly selected from an infinite population. In an experiment where three widths of spacing some crop are purposely selected for trial, it is not reasonable to regard these widths as random samples from all possible widths. On the other hand the blocks in a field experiment may sometimes quite reasonably be regarded as a random sample of all such blocks. In sampling production from say three machines in a factory, where these machines constitute all the machines which the factory has or is likely to have, it is more reasonable to regard these machines as the whole of a finite population than to consider them as random samples from some infinite population. If the factory owner is sampling production with a view to purchasing more machines of the same type, the three machines may be appropriately regarded as samples of the infinite population made up of all machines of the same type."

The more reasonable attitude to the three machines as the whole of a finite population is in fact a *Model I* view of the situation; but the same example also brings into focus a semantic difficulty which besets justification of the alternative view. Indeed, the preceding remarks of *Churchill Eisenhart* resolve only part of the difficulty of justifying the assumption that choice of classificatory variables is truly random. To be sure, we can choose cows of a particular herd at random, but if so, our assessment legitimately refers only to that herd. To extend it justifiably to others of the same breed we have to invoke the additional assumption that the range of

intraspecific variation does not materially differ from herd to herd; and to say that this assumption is itself unjustifiable deprives the assessment of public utility. In the nature of things, random choice of fertilisers of all possible chemicals curiosity or perversity may prompt the investigator to add to the soil is a concept devoid of operational meaning, and random choice of varieties within a species or of individuals within a variety is a concept we can justify without recourse to a God's-eye view of the universe only as a description of a local set-up. For a truly random choice of rabbit varieties in Kent would not be a truly random choice of rabbits in Kentucky.

In what has gone before, our concern has been to shew that the additive principle is a *sufficient* condition of the validity of the procedures involved in constructing a balance sheet of variance; but the argument of this section proceeds on the assumption that it is also a *necessary* one. That we are entitled to make this assumption becomes apparent, if we examine the implications of a semantic issue raised in § 1.

To say that such and such a fraction of total variance is attributable to a particular source is meaningful only in so far as it signifies how much reduction of total variance would result from eliminating the source, and such an assertion is itself meaningful without qualification only if there is no ambiguity in what elimination signifies in the same context. There is in fact no ambiguity, if we are entitled to assert that the reduction of total variation would be the same if we drew our r row sub-samples from any one of the r sub-universes specified by the row criterion or if we drew our c column sub-samples from any one of the c sub-universes specified by the column criterion of classification.

This must necessarily be true, if the score distribution of each sub-universe has the same variance. The additive postulate guarantees this condition, since it implies the existence of a set of score distributions different only with respect to constants involving a shift of origin. Needless to say, we can conceive an assemblage of different universes each with the same variance and the same mean if we postulate different laws of distribution; but if our significance tests invoke the provision that each sub-universe is a normal one, we can conceive them as both different and homoscedastic only in virtue of different mean score values. Additivity is indeed a necessary postulate of a meaningful causal partition of variance, if we assume any formal law of distribution common to each sub-universe.

The semantic issue raised in the last two paragraphs is not trivial, since it is possible to find in contemporary literature statements attributing the parentage of analysis of variance to the Lexis distribution. The score distributions of the Lexis universe are binomial variates; and the sub-universes do not constitute a homoscedastic system. It is indeed possible to effect a causal partition of variance within such a universe, only if we agree to adopt an arbitary definition of what we mean by removing the source of variation.

7. *Conclusions.*

1. Since the taxonomic framework fixes the terms of reference of any conclusions legitimately deducible from statistical analysis, an exhaustive breakdown of population variance exhibiting the overall contributions of nature, nurture and errors of observation is an unduly ambitious undertaking.

2. Any meaningful breakdown of population variance restricted to the evaluation of the contribution of particular classes of environmental or particular classes of genetic variables must:

(a) rely on particular postulates with respect to composition of the score;

(b) specify a particular operational framework within which the experiment is a representative sample;

(c) invoke certain statistical assumptions relevant to the assessment of error to which the constituent estimates are subject.

3. An operational framework which prescribes no *between-sample* variation of the row and column factors of a set-up involving one class of genetic and one class of environmental variation excludes the possibility of (c) and thus deprives a balance sheet exhibiting components of variance referable to one and the other of statistical precision.

4. Though the alternative assumption leaves the door open to the postulate of randomisation with respect to relevant row and column variables, the scope and design of experimental enquiry in which the nature-nurture issue is paramount commonly, if not invariably, exclude the validity of the postulate itself.

5. As regards the composition of the score, the assumption most extensively investigated hitherto is the principle of additivity, and biological experience provides many striking examples of situations to which the principle is grossly inapplicable.

6. By replication it is possible to show that there is no significant departure from additivity of row and column factors in accordance with the null hypothesis that there is no *systematic* cell to cell variation; but the interpretation of the result is ambiguous if the test fails to accredit the null hypothesis.

7. In the context of the nature-nurture issue the inclusion of a component of interaction in the balance sheet of variation on the basis of one such replication is consistent with two possibilities: (a) that the additive postulate is inappropriate and the balance sheet invalid on that account: (b) that repetition has disclosed a new, and conceivably additive, systematic component.

8. To prove that the new component is itself additive, it is necessary to complicate the design of the experiment by replications to demonstrate zero interaction on three levels. It is therefore misleading to speak of it as a component of interaction, if entitled to take its place as a meaningful item in an accredited balance sheet.

Résumé.

Toute décomposition de la variance de la population tendant à évaluer les contributions de certaines classes de variables extérieures et de certaines classes de variables génétiques, doit

a) être basée sur certaines hypothèses concernant le mode de composition des quantités observées;

b) spécifier un cadre dans lequel l'expérience est un échantillon représentatif;

c) recourir à certaines hypothèses statistiques en vue de déterminer les erreurs des estimations.

En ce qui concerne le mode de composition des quantités observées, la supposition qui a été le plus souvent étudiée jusqu'ici est le principe de l'additivité. L'expérience biologique a fourni de nombreux et frappants exemples dans lesquels ce principe est indubitablement inapplicable.

Zusammenfassung.

Jede sinnvolle Aufspaltung der Streuung der Grundgesamtheit zwecks Ermittlung des Anteils einzelner Klassen von Umwelts- oder von genetischen Faktoren, muß:

a) sich auf besondere Postulate hinsichtlich der Zusammensetzung der beobachteten Größe stützen;

b) einen besonderen Rahmen festlegen, innerhalb dessen das Experiment eine repräsentative Stichprobe darstellt;

c) gewisse statistische Voraussetzungen betreffend die Bestimmung der Fehler machen, denen die Schätzungen unterworfen sind.

Biologische Untersuchungen ergaben zahlreiche Beispiele, die schlagend dartun, daß die bis dahin am häufigsten gemachte Annahme der Additivität der Wirkungen nicht anwendbar ist.

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MORTALITY IN NORWEGIAN MENTAL HOSPITALS 1926–1941

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1. Introduction.

The excess mortality of the insane is a well known fact, and it has been studied in detail by *Malzberg*, *Alstrom* and *Ødegård*. These three investigations were all of them carried out on entire state hospital populations, that is: on all patients resident in certain hospitals during a certain period under investigation. The present study is, on the other hand, based upon successive first admissions only, with the exclusion of re-admissions. This method was chosen with the intention of studying the possible influence upon the excess mortality of the duration of the hospital stay—a point of considerable interest, which was noticed by Pollock, but which has not been studied in detail.

The material consists of all first admissions to Norwegian mental hospitals, public as well as private ones, during the period of 1916–1940. These cases were observed from 1926 through 1941. The reason for including patients admitted during the ten years previous to the actual period of observation, was that in this way the number of cases of long duration is increased. During the period under investigation there were 21,522 first admissions, giving a total number exposed to risk of 67,696.5. The number of deaths were 3370. Table 1 gives a general survey of the material and of the corresponding Norwegian population and its mortality.

2. Statistical method.

The number exposed to risk was calculated by the method of mean age and mean duration. The use of accurate ages and durations might have been preferable, but in our case the gain would hardly have been equal to the tremendous increase of work. It was felt, however, that some method of control was desirable. Therefore the number of years under observation (no. exposed to risk) was determin-

Table 1. General survey of the material.

Age	Mental hospitals				Total population of Norway				
	No. exposed to risk		No. of deaths		No. exposed to risk		No. of deaths		Central rates per
	Male	Female	Male	Female	Male	Female	Male	Female	Male
15–19	736	559	16	20	2,101,520	2,033,822	5,558	4,819	26.4
20–24	2,832	1,753	96	86	1,935,053	1,923,921	8,774	6,437	45.3
25–29	5,057.5	3,046	125	136	1,752,323	1,812,133	8,411	6,864	48.0
30–39	11,945.0	8,622.5	340	313	3,008,286	3,203,653	14,397	12,455	47.9
40–49	8,071.5	7,671	273	308	2,300,885	2,531,179	14,466	13,184	62.9
50–59	4,436	5,198	250	322	1,744,960	1,985,139	19,698	18,685	112.9
60–69	2,350.5	2,658.5	217	259	1,255,995	1,498,687	31,784	30,700	253.1
70–79	888.5	1,346.5	211	217	744,584	954,036	46,497	52,493	624.5
80–89	207	287	72	90	238,770	329,668	38,324	48,276	1,597.6
90–99	10.5	20.5	9	7	20,531	33,514	7,666	11,524	3,742.3
100–	0	0	0	0	366	793	142	309	3,879.8
Age unknown	—	—	0	2	—	—	249	82	—
Total	36,534.5	31,162	1,609	1,760	15,103,273	16,306,545	195,784	205,775	—

ed even according to a second method: by the use of accurate durations (in months), but disregarding age altogether. This is comparatively easily done, and it is sufficiently accurate under the assumption that the error induced by the use of mean duration is independent of age. As this way of checking the two methods has not been much discussed previously, the results may be of interest even apart from the present investigation.

It turned out that the method of mean duration led to a slight but systematic underestimation of the number of years under observation. This error is most marked for the first year of the hospital stay, and it disappears from the third year. The explanation is simple: Admissions and discharges are fairly evenly distributed over most of the year, but around the critical point of New Year this is not the case, because of the Christmas holidays. Patients as well as relatives are generally pressing to get the discharge before Christmas, and inversely admissions tend to be postponed until after the holidays if it is in any way possible. Table 2 shows that the number of discharges is actually disproportionately high in December, as against a decided minimum in January. Table 3 shows

Table 2. Sample of patients discharged within 12 months of admission, by month of discharge.

x	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sep.	Oct.	Nov.	Dec.	Total
en	104	105	112	137	141	141	143	132	147	143	129	142	1576
omen	126	138	137	149	157	151	163	152	153	157	154	176	1813
otal	230	243	249	286	298	292	306	284	300	300	283	318	3389

that this factor is of importance in recent cases only: after a couple of years the family ties are weakened. It is most important in diagnostic groups with a fair prognosis, and in manic-depressive and allied cases the error amounts to 2.5 to 4.7 percent, while for schizophrenia it is noticeable in men only, and for imbeciles, seniles and paretics there is no significant difference between the two methods.

This error is probably of greater importance in hospitals, such as tuberculosis sanitoriums, in which the patients stay for shorter

Table 3. Number exposed to risk as calculated with exact duration—in percent of the figures obtained by the method of mean duration.

	Diagnosis	1	2	3	4–5	6–10	10–
Men	Schizophrenia	101.5	100.5	100.7	100.7	99.9	99.9
	Manic-depression	104.1	104.7	99.1	100.9	99.3	99.1
	Constitutional ps.	102.4	102.6	98.1	99.9	99.3	100.3
	Senile and arterioscl.	102.9	100.2	100.5	99.2	101.2	100.0
	W. mental deficiency	99.9	100.3	99.5	99.0	100.0	99.5
	General paresis	100.7	101.2	99.0	99.9	100.2	99.6
	Remaining diagnoses	99.5	98.1	100.6	99.6	100.1	100.0
	All diagnoses	101.3	100.8	100.3	100.4	99.9	99.9
Women	Schizophrenia	100.1	100.7	99.9	100.1	99.5	100.4
	Manic-depression	102.5	99.8	98.4	97.1	99.6	—
	Constitutional ps.	103.7	100.2	100.3	99.3	100.9	99.8
	Senile and arterioscl.	99.1	99.5	98.6	99.7	99.5	100.9
	W. mental deficiency	99.7	100.4	102.3	101.0	100.6	—
	General paresis	100.4	99.9	99.8	100.3	100.0	—
	Remaining diagnoses	99.5	101.5	99.5	99.5	99 9	101 3
	All diagnoses	100.5	100.6	99.8	99.9	99.6	100.6

periods of time, and from which they much more effectively maintain contact with their homes. Even in the present material it is sufficiently important to justify the introduction of a correction, at least when various durational groups are compared.

* * *

Central death rates were calculated for separate age groups of five to ten years, and by dividing these rates with the corresponding rates for the general population of Norway, one arrives at *relative mortalities* which express the excess mortality of the insane. In most tables these relative mortalities alone are given, as tables including all data would become rather involved. For each relative mortality a corner numeral in small print gives the no. of hospital deaths upon which the calculation is based.

In many instances it seemed desirable to calculate a total excess mortality for all age groups together. This was generally done by the method of calculated numbers. This method was preferred, because it seemed safer than the standard population method, in view of the comparatively small number of cases in many of the groups. The method has its limitations when it comes to comparing different patient groups, such as the diagnostic groups of table 4. This table shows, for instance, that male schizophrenics have a relative mortality of 3.2, which means that for all age groups put together their mortality is 3.2 times as high as that of a group of average Norwegians *with the same age distribution* as these patients. With a patient group of higher age, a figure somewhat lower than 3.2 would have been the result, even though the relative mortalities of all individual age groups be exactly the same—namely because the relative mortality tends to decrease with age. This means that whenever two patient groups are compared, the group with the higher age is at an advantage with regard to relative mortality. If the difference in age distribution is too great, such as between schizophrenics and seniles, a comparison is senseless. When the difference is moderate, a comparison is justified, provided the relative mortality of the "younger" group be regarded as a maximum figure and that of the older group as a minimum figure. If, for instance, the male schizophrenics, with a mean age of 37.7 years, are compared with the male manic-depressives with their mean age of 49.5 years, the excess mortality of the former is actually over-estimated and that of the latter is under-estimated. Consequently the difference bet-

ween these two groups (which is exactly 0.52 ± 0.38) is actually under-estimated. In other cases an over-estimation of the difference will result, as for instance when the schizophrenics are compared with the somewhat younger imbeciles with their higher relative mortality.

The standard population method would eliminate this source of error. But apart from the new and unpredictable (random) errors introduced by smaller numbers, the advantages of this method are perhaps in our case somewhat theoretical. The results are bound to vary according to the age distribution of the standard population which is chosen, and it is not possible to find a standard which will not prove definitely unsuitable for some of the groups to be compared. After all, what we are after is the excess mortality of patient groups *as they are observed in our hospitals*, and not of non-existing groups with quite different age distributions.

Furthermore it seems (as will be shown later) that the excess mortality is actually more dependent upon duration than upon age, and consequently any standardization based upon age is somewhat beside the point. The conclusion is that whenever the method of calculated numbers is employed, all comparisons should be made with due consideration of the possible influence of age and duration, and whenever possible the comparison should be based upon individual age and durational groups.

The *psychiatric classification* is that which is official for all Norwegian mental hospitals. The term "constitutional psychoses" (actually "psychosis ex constitutione") needs an explanation: This group contains more or less reactive psychoses of hysterical, depressive or paranoid type which occurs in more or less constitutionally psychopathic individuals. In practice it tends to include a number of cases in which the diagnostic choice of schizophrenia or manic-depressive psychoses seems doubtful. It also includes the small group of paranoia.

In group 6 symptomatic psychoses of various clinical pictures are included, but the majority of the cases are confusional. Also included are a number of confusional cases of doubtful origin—possibly confusional forms of schizophrenia or mania which are not diagnosed as such. The group is of importance because of its excessively high mortality.

The causes of death are those of the international classification. Causes which in practice cannot be differentiated with any very

high degree of accuracy, are sometimes pooled. No attempt is made, for instance, to distinguish between broncho- and lobar pneumonia. Arteriosclerosis and apoplexy are for most purposes added to the group of "debilitas senilis". The cases in which "insanity", exhaustion, marasmus etc. are given as causes of death, are classified under "indefinite and unknown causes", and not under diseases of the nervous system.

The standard error of the calculated number of deaths is determined in the usual way as the weighted mean of the standard errors for the ten age groups. The standard error of the observed number of deaths is calculated (disregarding the age distribution) according to the usual formula for binomial distributions. In practically every instance the mortality of the insane is so much higher than that of the general population that the statistical significance of the difference is self-evident. Standard errors are therefore principally used for the comparison of relative mortalities for various groups of the material. The standard error of a relative mortality $\frac{x}{y}$ is calculated from the standard errors of the number of deaths observed (x) and that of the calculated number of deaths (y) according to the formula: $s_{\frac{x}{y}} = \frac{x}{y}\sqrt{\frac{s_x^2}{x^2} + \frac{s_y^2}{y^2}}$. In practice s_y can safely be left out, as it is insignificantly small in comparison with s_x. The formula is then reduced to $s_{\frac{x}{y}} = \frac{s_x}{y}$.

3. *The relative mortality in various psychoses.*

The excess mortality is naturally high for general paresis and for psychoses associated with epilepsy and with organic brain disease. It is excessively high for the confusional group—partly because these psychoses may be based upon some somatic illness with a high mortality such as renal or cardiac disorders. But no doubt confusion in itself is a danger to life, even if it is not stricly "symptomatic". Besides a number of highly acute cases are classified in the confusional group simply because death occurs before a more exact diagnosis can be made, and because the fulminant clinical picture is highly suggestive of some somatic disease. The excess mortality in the small group of "other and unspecified cases" probably has a similar

explanation, and besides this group undoubtedly includes many questionable organic cases of very high mortality.

Among the more or less "functional" psychoses manic-depression shows a somewhat higher excess mortality than schizophrenia. In alcoholic and constitutional psychoses it is low—probably because these groups include many patients who are psychopathic rather than psychotic, and who show a fairly normal behaviour in the hospital.

For most psychoses the excess mortality is higher in women than in men. Senile and arteriosclerotic psychoses form the only exception with a difference of 1.8 ± 0.35 in favour of the women.

A detailed analysis meets with the difficulty connected with differences in age distribution and duration, which was discussed above. It is quite evident that very high relative mortalities cannot be expected in the higher age groups, and the figures given for senile

Table. 4. Relative mortality of the insane by sex and diagnosis.

, as in all subsequent tables, the corner numerals in small print indicate the number of hospital s upon which the corresponding relative mortality is based. Each "relative mortality" is calcul- by dividing the death rate of the mental hospital patients with the death rate in a corresponding group of the normal population of Norway.

Diagnosis	All durations				First year of obs. only			
	Males		Females		Males		Females	
	Relative mortality	Mean age	Relative mortality	Mean age	Relative mortality	Mean age	Relative mortality	Mean age
ophrenia	618 3.2	37.7	709 4.8	40.8	125 5.1	32.6	159 7.5	36.0
c-depression	94 3.8	49.5	192 6.2	48.8	49 8.9	44.5	88 12.0	44.1
itutional	46 2.6	43.3	82 4.5	43.5	22 5.9	39.8	45 8.9	42.2
and arteriosclerotic	331 5.9	71.2	397 4.1	69.6	222 9.9	70.4	204 6.8	68.5
mental deficiency	62 3.5	37.2	64 6.5	36.7	14 5.1	31.7	22 11.6	33.0
tomatic (confusional)	41 53.8	39.5	98 44.2	43.2	39 95.5	36.6	93 123.9	39.9
olic	15 1.9	50.0	2 (3.7)	48.9	5 3.6	45.0	1 (5.5)	45.3
al paresis	271 19.2	44.8	99 28.9	44.2	127 35.3	43.4	50 39.5	44.2
ptic	50 7.1	38.7	39 13.9	38.2	16 18.8	32.6	17 28.7	33.9
ic	70 13.8	45.8	57 14.8	49.2	44 26.3	46.1	37 29.8	46.0
and unspecified	11 6.2	48.6	19 14.3	43.9	10 25.4	39.6	15 36.0	41.0
All diagnoses	1609 4.7	40.0	1758 5.5	43.4	673 10.0	37.2	731 10.4	40.9

psychoses can therefore not be compared with the rest. The influence of duration is illustrated by the right half of the table, which gives the relative mortalities for the first year in hospital alone. In these acute stages of mental illness, the excess mortality is generally twice as high as in the total material. The ranking order of the various psychoses remains very much the same, but the difference between schizophrenia and manic-depression is definitely larger. Evidently we can get no clear and complete picture of the influence of mental illness upon mortality unless age groups and durational groups are studied separately.

4. Excess mortality of the insane in relation to age and duration.

Previous investigations have shown that the excess mortality of the insane decreases with age. In the very high age groups this may be a statistical artefact: Owing to the high natural mortality in these age groups, one cannot expect these mortalities to be multiplied to the same extent as is possible in younger ages. But the decrease is evident even before the age of 40, and so even other factors must be at work. Table 5 seems to show that the decrease is most marked in diagnostic groups which include a large number of chronic cases, such as schizophrenia and psychoses with mental deficiency, which points to duration as a factor of importance. Table 6 confirms this in a very decided way: In all diagnostic groups the excess mortality tends to be highest in the first year of hospital treatment. The decline is very marked from the first to the second year, and from then on it continues more slowly.

The figures given in table 6 are based upon calculated numbers of deaths, and are consequently biased, because the age of the patients will naturally be higher in chronics than in acute cases. In table 7, figures are therefore given which are based upon standardized mortality rates. For each of the three most important diagnostic groups the total number (male and female) exposed to risk in this particular group is used as a standard, and so the influence of age is effectively removed. As might have been expected this procedure reduces the influence of duration somewhat, but it does not change the general picture.

Evidently age and duration are both important factors, and the crucial point is the interplay of these two factors, which is illustrated in table 8. In order to secure a sufficient number of cases in all the groups, a subdivision by psychiatric diagnosis must be omitted—but

Table 5. Relative mortality of the insane by diagnosis and age.

	Diagnosis	15–19	20–24	25–29	30–39	40–49	50–59	60–69	70–79	80–89	90–99	All ages
Men	Schizophrenia	9 7.2	72 7.6	99 5.2	205 4.6	102 2.9	71 2.5	43 1.7	14 0.9	2	1	618 3.2
	Manic-depression		2	4 13.7	10 7.9	15 7.8	25 7.0	21 2.6	14 1.8	2	1	94 3.8
	Constitutional			1	4 1.8	10 3.1	14 3.8	12 2.4	4 1.9	1		46 2.6
	Senile					2	21 32.6	75 8.8	160 6.5	67 3.2	6 4.0	331 5.9
	W. mental deficiency	12 12.5	10 7.5	6 3.3	17 4.9	9 3.3	7 1.8	6 2.1	3 2.6			62 3.5
	General paresis	1	1	4 31.5	67 33.8	99 25.5	68 16.0	27 10.4	4 3.6			271 19.2
	Epileptic, organic	2	9 18.3	8 13.5	22 18.4	20 13.2	30 13.3	21 8.9	7 5.8		1	120 10.0
	Confusional, alcoholic and others		2	3	15 18.1	16 15.1	14 5.6	13 2.9	5 2.8			67 6.4
	All diagnoses	16 8.3	96 7.9	125 5.5	340 6.2	273 5.5	250 5.1	217 3.7	211 3.8	72 2.2	9 2.3	1609 4.7
Women	Schizophrenia	9 11.8	62 14.6	95 10.6	201 7.6	158 5.3	100 3.3	53 2.2	21 1.3	10 1.7		709 4.8
	Manic-depression			8 18.0	21 12.5	34 10.7	89 9.6	39 4.7	19 2.2	1		192 6.2
	Constitutional	1	3 8.6	8 11.1	13 6.6	12 3.0	26 5.4	15 5.0	3 1.3		1	82 4.5
	Senile and arteriosc.					4 30.5	33 16.9	114 7.7	161 3.8	79 2.5	6 0.9	397 4.1
	W. mental deficiency		8 13.2	13 13.7	15 7.8	9 5.4	13 8.1	3 2.0	3 2.2			64 6.5
	General paresis	1	5	2	15 32.0	37 43.8	31 25.7	7 11.2	1			99 28.9
	Epileptic-organic	2	5	4	21 27.8	21 28.7	20 17.9	15 11.7	8 4.4			96 14.4
	Confusional, alcoholic and others	6	3	6 41.0	27 67.5	33 48.6	30 38.2	13 21.2	1			119 29.2
	All diagnoses	20 15.1	86 14.8	136 11.8	313 9.4	308 7.7	322 6.6	259 4.8	217 2.9	90 2.2	7 1.0	1758 5.5

Table 6. Relative mortality of the insane according to diagnosis and duration of hospital stay (in years).

	Diagnosis	1	2	3	4–5	6–10	11–25
Men	Schizophrenia	125 5.1	93 5.0	77 4.1	103 3.8	123 2.3	97 1.9
	Manic-depression	49 8.9	9 3.9	6 3.0	9 2.9	10 1.6	11 2.0
	Constitutional	22 5.8	4 1.7	4 2.2	3 1.1	7 1.8	4 3.0
	With mental deficiency	14 5.1	7 3.6	9 5.3	15 5.9	13 3.0	4 0.9
	Senile and arteriosclerotic	222 9.8	37 3.9	29 4.5	23 3.2	14 1.7	6 2.6
	General paresis	127 33.5	54 24.4	32 20.7	31 14.1	20 6.4	7 6.0
	Epileptic and organic	60 23.8	14 9.2	9 6.8	15 6.6	11 4.0	11 6.5
	Confusional, alcoholic, others	54 24.9	<	6 2.1	>	7 1.3	
	All diagnoses	673 10.0	220 5.6	169 5.4	200 4.1	201 2.4	146 2.0
Women	Schizophrenia	159 7.5	106 7.1	80 6.2	118 5.4	162 3.9	84 2.3
	Manic-depression	88 12.0	30 8.0	16 5.9	12 3.0	31 4.4	15 2.4
	Constitutional	45 8.8	8 3.3	7 3.9	5 2.2	10 2.5	7 2.7
	With mental deficiency	22 11.6	8 6.3	6 6.4	7 4.6	15 5.3	6 4.2
	Senile and arteriosclerotic	204 6.8	64 3.8	27 2.1	54 3.3	38 2.5	10 1.5
	General paresis	50 39.8	16 22.0	17 33.2	12 27.8	– 4 8.4 >	
	Epileptic and organic	54 29.4	12 12.5	5 6.0	15 12.3	< 10 5.5 >	
	Confusional, alcoholic, others	109 80.7	<	8 7.3	>	< 2 1.2 >	
	All diagnoses	731 10.4	249 6.0	161 5.0	223 4.6	269 3.7	125 2.4

Table 7. Relative mortality of the insane by diagnosis and duration—based upon standardized mortality rates.

	Diagnosis	1	2	3	4–5	6–10	11–25
Men	Schizophrenia	4.6	4.1	4.2	3.2	2.4	2.3
	Manic-depression	7.2	3.7	2.5	2.6	1.9	1.9
	Senile and arteriosclerotic	9.6	3.6	4.7	3.2	1.5	2.3
	All diagnoses	10.6	5.5	5.3	3.8	2.3	2.2
Women	Schizophrenia	6.3	6.0	5.0	5.0	4.5	2.9
	Manic-depression	10.3	7.4	5.3	3.0	5.5	3.3
	Senile and arteriosclerotic	6.5	3.8	2.2	3.4	2.3	1.6
	All diagnoses	10.5	6.0	4.8	4.5	3.6	2.7

this seems to be permissible in view of the findings in tables 6 and 7. All organic and epileptic psychoses as well as general paresis are excluded, however, because of their excessively high mortality from causes specifically linked with the psychosis itself.

Table 8. Relative mortality of the insane according to age and duration. All diagnoses, except general paresis, organic and epileptic psychoses. All causes of death.

	Age	1	2	3	4–5	6–10	11–25	All durations
Men	15–29	64 6.1	43 6.4	30 5.9	45 6.9	28 4.6	2 (2.7)	212 6.0
	30–39	59 6.6	29 4.7	30 5.6	53 6.0	52 3.4	28 3.5	251 4.8
	40–49	53 9.4	16 4.0	16 4.5	11 1.7	27 2.2	31 2.6	154 3.5
	50–59	63 10.3	17 4.3	14 4.2	18 3.1	17 1.5	23 1.8	152 3.5
	60–69	86 8.7	20 3.7	11 2.5	11 1.5	23 1.7	18 1.4	169 3.1
	70–99	161 7.8	27 2.8	27 3.9	16 1.7	23 1.2	26 1.2	280 2.4
	All ages	486 7.9	152 4.2	128 4.5	154 3.5	170 2.2	128 1.9	1218 3.8
Women	15–29	86 13.8	33 10.0	40 16.9	35 11.3	25 9.0	4 13.1	223 12.3
	30–39	90 12.7	38 8.6	23 6.6	38 6.9	71 8.6	17 4.9	277 8.6
	40–49	94 13.5	29 6.5	16 4.3	32 5.3	52 5.0	27 3.9	250 6.5
	50–59	122 13.7	36 6.9	24 5.6	27 3.9	37 3.2	25 2.6	271 5.8
	60–69	107 10.0	42 6.6	16 3.2	21 2.9	34 2.7	17 1.6	237 4.5
	70–99	128 4.7	43 2.7	20 1.6	43 2.4	38 1.5	33 1.5	305 2.5
	All ages	627 9.4	221 5.5	139 4.5	196 4.2	257 3.6	123 2.4	1563 5.1

The table shows that during the first year in hospital the excess mortality is largely independent of age. But as the years pass on, the influence of age tends to become more marked, and in chronics it is very definite. Inversely the patients under 30 years of age have a very high excess mortality which is independant of duration. During the thirties the influence of duration comes into evidence, and it seems to be most marked above the age of 50.

The mixture of very heterogeneous diagnoses in table 8 is naturally unfortunate. In table 9 the corresponding data are therefore given for the only diagnostic group in which an approximately sufficient number of cases can be mustered, namely schizophrenia. The general picture is the same as in table 8. One should bear in mind that above the age of 60 very high excess mortalities are

Table 9. Relative mortality of the insane according to age and duration. Schizophrenia. All causes of death.

	Age	1	2	3	4–5	6–10	11–25	All durations
Women	15–29	54 12.1	28 10.7	33 17.2	31 12.4	19 8.5	1 (4.5)	166 11.9
	30–39	40 7.9	32 8.9	19 6.5	34 7.1	62 8.7	14 4.9	201 7.6
	40–49	29 7.2	21 6.7	15 5.3	29 5.9	41 4.6	23 3.8	158 5.3
	50–59	21 6.8	13 4.7	8 3.0	18 4.0	20 2.6	20 2.5	100 3.3
	60–69	10 4.3	10 5.1	3 1.8	3 1.0	16 2.2	11 1.3	53 2.2
	70–99	5 3.3	2 2.1	2 2.2	3 1.4	4 0.6	15 1.5	31 1.4
	All ages	159 7.5	106 7.1	80 6.2	118 5.4	162 3.9	84 2.3	709 4.8
Men	15–29	46 5.4	40 6.9	25 5.8	42 7.4	25 4.8	2 0 3.5 9	180 6.0
	30–39	36 5.5	28 5.4	26 5.7	42 5.5	47 3.5	26 3.9	205 4.6
	40–49	18 5.1	10 3.5	12 4.4	11 7.5	23 2.2	28 2.7	102 2.9
	50–59	16 5.9	9 4.1	8 4.1	7 2.0	12 1.5	19 1.9	71 2.5
	60–69	6 3.0	4 2.7	4 3.0	1 —	14 1.7	14 1.5	43 1.7
	70–99	3 2.5	2 1.7	2 2.2	- —	2 —	8 0.6	17 0.7
	All ages	125 5.1	93 5.0	77 4.1	103 3.8	123 2.3	97 1.9	618 3.2

statistically impossible, and therefore the figures tend to exaggerate the influence of age in these groups. Also we recall that the relative mortalities found for the first year are somewhat too low, owing to a systematic error (which is less than 2 percent, however). One might therefore venture the conclusion that duration is probably the more important of the two factors, but that age is decidedly not without its influence. A closer analysis must be referred until the causes of death can be considered.

5. The excess mortality from various causes of death.

The statistical registration of causes of death is uncertain. Even if the medical diagnosis is clear, classification is to some extent a matter of personal opinion, which is particularly true when it comes to the definition of „primary" and „secondary" causes of death. A comparison of statistical material from two different sources should therefore be made with great caution, unless the two groups of deaths have been registered under closely similar conditions. This is not the case when the deaths in mental hospitals are compared with the total deaths in Norway, because the latter have in a majority

of the cases taken place outside of hospitals. Systematic errors may result, and we have few means of guessing in which direction they are likely to go.

The excess mortalities from various causes of death are therefore given with reservations. The errors are probably less important when the problem is to examine the variations of excess mortality according to age, duration and psychiatric diagnosis. But here we encounter the difficulty that the material is insufficient for a subdivision by all these factors simultaneously. As a possible solution the material is therefore first subdivided according to cause of death and psychiatric diagnosis—then according to cause of death and age, and finally according to cause of death and duration. The results are given in tables 10, 11 and 12, and a brief discussion of the findings is given for each cause of death.

a) Organic diseases of the nervous system.

This cause of death predominates in general paresis, epileptic and organic psychoses, but apart from these "specific deaths" the

le 10. Relative mortality of the insane by cause of death, for main diagnostic groups.

Cause of death	Men								Women							
	Schizophrenia		G.-P., epileptic, organic		Remainig diagnoses		All psychoses		Schizophrenia		G.-P., epileptic, organic		Remanins diagnoses		All psychoses	
rculosis	360	8.0	30	7.2	74	6.4	464	7.6	402	12.8	11	6.6	128	11.2	541	12.2
iratory diseases	72	4.4	42	17.3	133	10.8	247	7.9	72	5.9	29	30.4	187	10.6	288	9.1
tious diseases	30	3.9	8	8.4	24	7.3	62	5.2	26	5.2	—		41	11.2	67	7.5
latory diseases	17	1.0	14	5.2	54	3.9	85	2.6	38	2.3	5	4.0	71	3.5	114	3.0
ro-intest. diseases	23	2.4	6	4.5	28	5.6	57	3.6	35	5.1	7	15.3	35	6.1	77	5.9
to-urinary diseases	5	0.5	10	6.5	22	2.6	37	1.9	10	1.4	5	10.5	31	5.6	46	3.5
nic nervous diseases	4	0.8	248	393.0	6	1.7	258	33.7	9	2.9	120	632.0	17	9.5	146	28.6
riosclerosis	3		8		46	5.4	57	4.0	2		1		35	3.7	38	3.0
plexy	10	0.9	9	4.4	53	4.3	72	3.0	10	1.2	2	3.0	55	2.8	67	2.1
e debility	6		0		77	6.3	83	4.4	11		2		136	5.5	149	5.0
ours	24	1.0	3	0.7	28	1.6	55	1.2	31	1.1	3	1.5	27	1.0	61	1.1
atural death	24	1.1	8	3.3	21	3.1	53	1.7	9	3.2	9		26	12.6	37	7.4
r known causes	10	2.3			6	2.2	16	2.1	12	1.5	2		13	2.4	27	1.9
e of death indefinite unknown	30	3.2	5	3.4	28	4.0	63	3.5	40	6.3			58	7.8	08	7.0

Table 11. Relative mortality of the insane by cause of death and age. All diagnoses except general paresis, epileptic and organic psychoses.

Cause of death	Men						Women					
	15–29	30–39	40–49	50–59	60–69	70–99	15–29	30–39	40–49	50–59	60–69	70–99
Tuberculosis	166 9.2	149 7.2	56 5.8	34 7.7	21 7.5	9 7.4	160 14.1	157 11.1	98 12.1	67 14.2	31 11.6	17 8.4
Respiratory diseases	15 7.4	26 6.7	15 3.6	31 7.0	43 8.3	76 8.2	19 22.5	28 12.4	33 11.0	51 11.6	58 10.3	70 4.7
Infectious diseases	4 2.3	17 6.3	11 4.8	8 5.1	8 5.9	6 4.5	7 8.4	14 9.1	23 14.8	13 9.1	5 4.2	5 2.4
Circulatory diseases	2 1.8	6 2.5	14 3.5	12 2.2	17 2.1	20 2.2	5 6.6	13 5.5	16 3.8	27 4.3	21 2.5	27 1.8
Gastro-intestinal	5 3.0	6 2.1	18 6.1	9 3.6	5 2.1	8 3.6	6 9.5	14 8.9	16 7.3	17 6.8	13 5.3	4 1.2
Genito-urinary deseases	2	1	3	3	8 2.1	10 1.5	2	7 4.6	7 2.9	7 2.4	14 5.6	4 1.4
Organic nerve diseases	1	1	6	1	1	-	6 12.9	4 4.8	6 5.2	7 6.4	1	2
Arteriosclerosis			1	2	10 4.3	36 3.7				1	13 8.5	23 2.2
Apoplexy	1	2	1	15 4.7	18 2.8	26 2.4	-	1	6 3.3	13 2.7	21 2.7	24 1.5
Senile debility				1	14 22.4	68 4.0				6	33 38.1	108 3.8
Tumors		5 2.0	9 1.6	9 1.0	12 0.9	17 1.3	-	5 1.8	7 0.8	17 1.3	18 1.4	11 0.7
Unnatural death	5 0.7	13 1.4	10 1.6	8 2.3	6 3.0	3 2.6	3 6.3	5 6.0	9 9.6	9 11.4	3 5.3	6 4.9
Other known caus.		3	3	5	5	-	5	57	19	97	1	1
Cause of death indefinite or not given	10 13.2	17 9.3	11 4.4	13 4.5	3 0.8	4 0.9	9 27.0	22 24.0	27 17.1	29 13.3	7 2.5	4 0.7

Table 12. Relative mortality of the insane by duration of hospital stay and cause of death. All diagnoses except general paresis, organic and epileptic psychoses.

Cause of death	Men					Women				
	1	2	3–5	6–10	11–25	1	2	3–5	6–10	11–25
Tuberculosis	69 6.1	68 9.0	158 9.9	88 6.3	58 6.2	90 8.7	75 12.4	180 15.5	137 14.0	48 9.7
Respiratory diseases	118 21.7	19 6.0	33 5.2	16 2.2	16 2.4	149 22.6	29 7.5	35 6.6	29 4.1	12 2.2
Infectious diseases	32 15.9	5 3.8	10 3.7	7 2.5	5 2.3	53 28.4	10 8.9	6 2.7	4 2.0	8 5.8
Circulatory diseases	38 6.8	9 2.8	6 0.9	6 0.8	8 1.1	57 7.3	15 3.3	19 2.1	14 1.6	10 1.5
Gastro-intestinal diseases	20 7.7	7 4.2	7 2.1	8 2.1	9 2.8	23 8.6	14 8.9	7 2.2	15 4.9	6 2.8
Genito-urinary diseases	16 6.1	2 (1.0)	6 1.5	3 0.7	2 0.5	23 8.7	5 3.2	6 1.9	4 1.3	3 1.4
Ateriosclerosis	28 9.5	5 3.4	5 2.0	4 1.3	5 1.5	16 6.0	5 3.1	4 1.3	8 3.0	4 1.8
Apoplexy	33 7.6	12 5.1	10 2.2	2 0.4	4 0.7	28 4.2	13 3.4	12 1.6	6 0.8	4 0.7
Senile debility	54 12.5	6 3.1	14 4.2	5 1.5	2 0.4	57 8.8	27 6.3	35 4.7	11 2.0	12 2.3
Tumors	12 1.5	7 1.6	9 1.0	11 1.0	12 1.1	15 0.9	8 1.2	12 0.9	16 1.2	7 0.7
Unnatural death	24 4.5	6 1.6	8 1.0	5 0.7	3 0.6	20 18.7	3 4.7	7 5.6	2 1.8	3 3.9
Other known causes	6 2.4	2 1.3	6 1.8	7 1.9	5 1.6	27 6.2	5 2.1	5 1.4	3 0.7	3 1.0
Cause of death indefinite or unknown	33 11.2	3 1.7	9 2.5	7 1.7	8 2.1	67 22.6	12 7.1	8 2.4	7 2.2	3 1.2

excess mortality from nervous diseases is moderate, with the exception of non-schizophrenic women. But the number of cases is too low to warrant any conclusions, and besides errors of classification are very likely. No doubt schizophrenics or manics who die in acute confusional states may in some cases be diagnosed as encephalitis or meningitis owing to brain edema and hyperemia found by autopsy. Nearly all the cases of brain tumor, Huntington or Wilsons disease were admitted for psychoses due to these organic lesions, and so we do not find any evidence that diseases of this type show any increased incidence in the insane.

b) Respiratory diseases.

The excess mortality from respiratory diseases (which in practice means pneumonia) is independant of age, which corresponds with the findings for tuberculosis. But while tuberculosis is equally prevalent in acute and chronic cases, pneumonia seems to be definitely more frequent in the acute stages of mental illness. The moderate figures found for schizophrenia evidently is a result of the predominance of chronic cases in this diagnostic group, and the predisposition towards pneumonia is therefore not linked with any particular type of mental illness or with any special constitutional traits, but with symptoms and forms of behaviour which are characteristic of all forms of mental disorder in the acute stages. Our clinical experience with the bed-ridden and nearly motionless depressive with his lack of appetite and general vitality, or with the excited patient who is nearly naked in his poorly heated single room, makes this seem quite natural.

c) Infectious diseases.

The excess mortality is nearly as high as for respiratory diseases, and as for that group it is found to be independent of age, but rapidly decreasing with the duration of the disease. Evidently the mechanism is closely allied to that which was found for pneumonia.

A study of the nature of the infections shows that the situation in the mental hospital is quite different from that in the population as a whole. Deaths from epidemic diseases like typhoid and diphteria are less common, while septic infections, erysipelas and gastro-enteritis predominate. Evidently the personal hygiene of the patients is less satisfactory than the general epidemiological hygiene of the hospital, and here (as for pneumonia) the acute patient is the

real problem. The high incidence of gastro-enteritis points directly towards unsolved hygienic problems of the water supply and the kitchen departments of the hospitals.

d) Circulatory diseases.

Here again the excess mortality is independent of age, and much higher in the acute cases than in the chronic ones. It is particularly low in schizophrenics, who may be protected against circulatory disturbance by their less intensive emotional reactions and their physical inactivity. Apoplexy and arteriosclerosis are also relatively rare causes of death in schizophrenia.

e) Genito-urinary diseases.

The excess mortality is very low in schizophrenia, moderate in the non-schizophrenic psychoses, and rather high in the organic group—evidently because of the predisposition of the organics towards urinary infections. The decisive influence of the factor of duration is found even here.

f) Gastro-intestinal diseases.

The excess mortality from gastro-intestinal diseases is moderate. Chronic enteritis and colitis as well as ileus seem to be relatively common, while other forms of "acute abdomen" present few deaths. One might conclude that acute abdominal diseases are as a whole well taken care of in the mental hospitals, but that the eating habits of the patients and the high incidence of habitual constipation lead to frequent and serious intestinal malfunction.

g) Causes of death related to old age.

The present material does not make it possible to distinguish with accuracy between death from arteriosclerosis, apoplexy and senile marasmus or debilitas, and in the general population this is probably even more so. The figures seem to show that the excess mortality is highest for senile debility, and lowest for apoplexy. The mortality from senile debility is excessively high in the sixties—probably because of the pre-senile cases of the Pick-Alzheimer type, which have a very high mortality.

h) Tumors.

Our material confirms the findings of previous investigations, that cancer mortality is not raised in the insane, and that this is the only exception from the general rule of an excess mortality in

all mental patients. The younger age groups form a possible exception, but the number of cases is too small in these ages to allow any safe conclusions. The fact that this low cancer mortality is found in all diagnostic groups suggests environmental rather than constitutional factors, and the natural explanation seems to be that the poor nutritional state of a majority of our patients may be responsible. Now one should bear in mind that the cancer mortality, though relatively low, is nevertheless not lower in the mental patients than in the general population. The findings therefore can hardly be used in support of the nutritional theory of cancer, particularly as the low excess mortality is found in chronics as well as in relatively recent admissions.

i) *Other known causes.*

This mixed group comprises the metabolical and nutritional disorders, and shows a very low excess mortality. Among the ten cases of diabetes only 3 were classified as schizophrenics, which sems to confirm that these two diseases do seldom coincide.

j) *Cause of death unknown or indefinite.*

In the general population this group consists mainly of cases in which "paralysis cordis" or similar indefinite causes of death are given, and five sixths of them fall in the age groups above 50 years. In the mental hospitals the rule which forbids the use of such indefinite terms, is more strictly observed, and if no cause of death is actually established, formalities are at least observed by putting down "insanity" or some similar cause, which is statistically permissible. Nevertheless it would be misleading to classify these cases under diseases of the nervous system, where they belong according to the international classification. A majority of the deaths in this group occurred during periods of excitation or confusion, most frequently in the acute stages of the psychoses, and sometimes even before a psychiatric diagnosis could be made. These 161 cases represent more than 4 percent of the total number of deaths, and therefore represent an important source of error. Undoubtedly many of them are actually circulatory deaths, and so they possibly might have raised the comparatively low excess mortality from these disorders.

k) *Unnatural death.*

In mental hospitals most unnatural deaths are suicides, while in the general population accidents of various types prevail. The

patients are effectively protected against accidents connected with work and play, and so a comparison with the general population actually has little meaning. In this case the absolute rates for the hospital population are therefore preferable, as given in table 13. Of the 91 cases 62 are certain suicides, while the remaining 29 may or may not be accidents.

Table 13. Death rates per 1000 from unnatural death in mental hospital patients.

	Men			Women		
	No. of deaths	Exposed to risk	Death rate	No. of deaths	Exposed to risk	Death rate
Diagnosis						
chizophrenia	24	26,165	0.92	9	21,194.5	0.43
eneral paresis, organic and epileptic ps.	9	2,768.5	3.26	3	1,194.5	2.51
emaining diagnoses	21	7,610	2.76	25	8,773	2.84
Age at death						
0–29	5	7,889.5	0.63	4	4,799	0.83
0–39	14	11,945	1.17	5	8,622.5	0.58
0–49	15	8,071.5	1.85	9	7,671	1.17
0–69	17	6,786.5	2.51	13	7,856.5	1.65
0–99	3	1,106	2.72	6	1,654	3.63
Total	54	36,543	1.47	37	31,162	1.19

The total incidence is 1.47 per 1000 per year in men, and 1.19 in women. In schizophrenics alone is the incidence significantly higher in men, with a difference of 0.49 ± 0.21. The incidence of unnatural death is low in schizophrenia and high in the non-schizophrenic group, which includes the depressions. In both sexes the incidence tends to increase with age, and it is much higher in acute cases than in chronics (table 12).

Table 14 shows that strangulation is the most common form of suicide in mental hospitals. Drowning comes next, which is explained by the location of many of our hospitals close to the sea. The total number of unnatural deaths per year is 6, which is not too unsatisfactory for a population of more than 7000.

Table 14. Unnatural deaths in Norwegian mental hospitals 1926–40.

Cause of death	Schizo-phrenia		Senile and arterio.		General paresis		Organic, epileptic		Remaining diagnoses		To
	M	W	M	W	M	W	M	W	M	W	M
Strangulation	9	3	1		2				11	8	23
Drowning	5		1	1					3	4	9
Poisoning	1									1	1
Precipitation (out windows etc.)		2			2			1	1	1	3
Self-inflicted wounds										1	
Not specified	2									2	2
Certain suicides, total	17	5	2	1	4			1	15	17	38
Head injuries	2		1		2		2		1	2	8
Suffocation (food)	2				1	1				1	3
Poisoning (paraldehyde, cytisine)	1								1		2
Combustion		1						1			
Foreign bodies, intestinal tract	1	1									1
Fractura colli femoris		1		4							
Traumatic pneumo-thorax		1	1								1
Frozen to death after escape	1										1
Total accidents	7	4	2	4	3	1	2	1	2	3	16

Cause of death and sex.

The total excess mortality is somewhat higher in the female sex, but the ranking order of the various causes of death is about the same. In male patients apoplexy, arteriosclerosis and organic nerve diseases are relatively more important as causes of death, while in women tuberculosis, gastro-intestinal and genito-urinary diseases show a decided predominance. The most important difference is that found for tuberculosis, which is statistically significant beyond doubt, and which is the main reason for the higher excess mortality in the female sex. The difference found for unnatural deaths is a mere result of the fact that the incidence of unnatural deaths in the general population is much higher in men than in women (even when, as in the present material, the war casualties of 1940 are left out).

Cause of death and age.

As previously stated the total excess mortality tends to decrease with age. Table 11 seems to indicate that this tendency is less

evident for the separate causes of death. In most cases there is no evidence of any decrease at all below the age of 70, and even above that age it is not constant. This leads us to a new explanation for the decreasing age curve of the excess mortality: To a large extent it is due to the fact that the predominating causes of death of advanced age, such as circulatory and genito-urinary disorders, apoplexy, arteriosclerosis and cancer, have in general a comparatively low excess mortality. The excess mortality is very high, on the other hand, for tuberculosis, which is the predominating cause of death in the younger age groups in Norway.

Cause of death and duration.

Table 12 shows that for most causes of death the excess mortality is very high during the first year in hospital. From the first year to the second, there is a very marked decrease, which continues more gradually during the following years. In chronics, the excess mortality is uniformly low for all causes of death. The only exception is tuberculosis, which shows a maximum in the third to fifth year, and only a very moderate decrease in the chronic stages.

6. The excess mortality from tuberculosis.

In the present material 30 per cent of the deaths are caused by tuberculosis. This cause of death therefore deserves a somewhat closer analysis, and the number of cases makes this statistically possible. In the following tables the excess mortality from tuberculosis is compared with the total excess mortality from all other causes of death. Deaths from causes which are specific to certain diagnostic groups (that is: deaths from general paresis, epilepsy and organic brain disorder) are excluded, however. The method has, of course, its serious limitations, but it may serve to illustrate the relative importance of tuberculosis among the insane.

Table 15 shows that in both sexes and in practically all diagnostic groups tuberculosis has by far the highest excess mortality. This is particularly true of schizophrenia, while in the manic-depressive and constitutional groups the difference is more moderate.

Owing to the small number of cases in certain groups, a subdivision by age and duration is only possible for somewhat larger diagnostic groups. In table 16 schizophrenia and the three "specific" organic groups of paresis, epileptic and organic psychoses are singled

Table 15. Relative mortality of the insane from tuberculosis, by sex and diagnosis.

Diagnosis	Men		Women	
	Tuber-culosis	All other causes of death	Tuber-culosis	All other causes of death
Schizophrenia	361 8.0	257 1.8	402 12.8	307 2.7
Manic-depression	14 6.4	80 3.5	44 13.5	148 5.3
Constitutional psychoses	11 3.8	35 2.4	17 5.8	65 4.3
Senile and arteriosclerotic	14 12.7	317 5.8	18 8.9	385 4.0
With mental deficiency	27 6.3	35 2.6	34 13.0	30 4.2
Confusional (symptomatic)	7 39.5	34 58.4	12 42.6	86 44.5
Alcoholic psychoses	-	15 2.1	1	1
General paresis*)	11 4.7	67 5.8	3 4.8	21 7.5
Epileptic psychoses*)	12 9.4	17 3.0	7 10.1	10 4.7
Organic psychoses*)	7 13.1	25 5.5	1 02.9 9	27 7.7
Other and unspecified	1 05.7 9	10 6.3	2 08.2 9	15 15.7
All diagnoses	465 7.6	893 3.2	541 12.2	1097 4.0

*) Deaths from the "specific causes" of death (general paresis, epilepsy and organic brain disease) are excluded in this table.

out. The remaining cases are predominantly "functional" non-schizophrenic psychoses of various types. The table shows that in schizophrenia tuberculosis is the outstanding cause of death throughout the age groups, while in the non-schizophrenic functional psychoses the difference is very slight, and in women above the age of 50 the "other causes" even show the higher excess mortality. But this is not primarily due to a particularly high excess mortality from tuberculosis in schizophrenia, but rather to a very low excess mortality from "other causes of death" in this diagnostic group.

The most interesting feature of table 16 is that when tuberculosis is singled out, the decrease of excess mortality with age becomes less apparent. For tuberculosis no decrease at all is found, while for the remaining causes of death the decrease is slight and irregular. Evidently the decrease of excess mortality with age is to a large extent connected with the prevalence of tuberculosis in the younger age groups, which will naturally lead to a high excess mortality in these age groups.

Table 16. Relative mortality of the insane from tuberculosis and other causes of death, by age.

	Diagnosis	Cause of death	15–24	25–29	30–39	40–49	50–59	60–69	70–99	All ages
Men	Schizophrenia	Tuberculosis	64 11.7	82 8.3	131 7.5	47 6.1	25 8.4	10 7.5	2 (5.5)	361 8.0
		Other causes	17 3.3	17 1.8	74 2.8	55 2.0	46 1.8	33 1.3	15 0.6	257 1.8
	General paresis, epileptic and organic psych.	Tuberculosis	5 14.4	2 5.4	10 7.9	7 5.9	5 7.5	1 (3.9)	- —	30 7.2
		Other causes*)	2 5.5	5 14.2	18 9.4	34 7.9	28 4.8	20 4.3	3 0.7	110 5.0
	All other diagnoses	Tuberculosis	10 8.1	10 6.5	18 5.8	9 4.6	9 6.2	11 7.5	7 8.2	74 6.4
		Other causes	8 6.2	4 2.7	28 5.9	43 6.2	72 5.7	115 4.2	256 4.2	526 4.6
Women	Schizophrenia	Tuberculosis	58 17.7	70 12.8	113 11.5	82 13.0	39 12.8	14 11.3	6 16.1	402 12.8
		Other causes	13 7.5	25 7.2	68 4.6	76 3.2	61 2.2	39 1.7	25 1.1	307 2.7
	General paresis, epileptic and organic psych.	Tuberculosis	2 8.7	- —	4 7.4	2 6.0	3 12.8	- —	- —	11 6.6
		Other causes*)	2 16.4	2 16.4	10 14.6	15 12.1	16 7.7	9 5.0	4 1.8	58 6.9
	All other diagnoses	Tuberculosis	12 10.1	20 14.5	24 9.1	16 8.8	28 17.0	17 11.8	11 8.2	128 11.2
		Other causes	10 15.7	15 17.1	52 15.6	76 11.2	144 9.8	169 6.1	266 2.8	732 4.9

*) Deaths from the "specific causes" of general paresis, epilepsy and organic brain disease are excluded.

Table 17. Relative mortality from tuberculosis and other causes of death, according to duration of hospital stay.

	Diagnosis	Cause of death	1	2	3	4–5	6–10	11–25
Men	Schizophrenia	Tuberculosis	41 5.1	60 10.1	49 10.0	83 10.8	79 6.8	48 6.9
		Other causes	84 5.1	33 2.6	28 2.6	20 1.0	44 1.1	49 1.1
	General par., organic and epileptic psych.	Tuberculosis	9 7.6	7 9.9	3 5.8	4 6.1	4 5.4	3 8.7
		Other causes	178 34.1	61 20.2	38 16.2	42 11.0	27 5.3	15 6.0
	Remaining diagnoses	Tuberculosis	28 8.7	8 5.0	9 7.4	16 10.7	9 3.8	4 2.7
		Other causes	333 9.9	51 3.3	42 3.7	35 2.3	38 1.6	27 1.7
Women	Schizophrenia	Tuberculosis	52 8.1	58 13.5	66 19.1	81 15.2	106 13.7	39 9.7
		Other causes	107 7.2	48 4.5	14 1.5	37 2.2	56 1.7	45 1.4
	General paresis, organic and epileptic psych.	Tuberculosis	2 3.6	1 (3.3)	4 8.3		4 12.5	
		Other causes	102 40.1	27 19.5	45 17.9		10 5.1	
	Remaining diagnoses	Tuberculosis	38 9.8	17 9.8	18 14.9	15 9.3	31 15.3	9 9.5
		Other causes	430 10.3	98 4.3	41 2.4	63 2.7	64 2.3	30 1.8

Table 17 shows the influence of duration upon the excess mortality from tuberculosis and other causes of death, and here the difference is outstanding. For tuberculosis the excess mortality is very high during the first year in hospital, but it does not reach its maximum until the second or third year, and from then on it decreases slightly. But even in the most chronic cases it remains very high. For the remaining causes of death, on the other hand, we find a very marked decrease of the excess mortality from the first to the second year. There may be some further decrease during the next year also, but then the minimum is reached, and for cases of more than 3 years standing the excess mortality is independent of duration.

Table 18 a. Men. Relative mortality of the insane from tuberculosis and other causes of death according to age and duration. All psychiatric diagnoses, except general paresis, organic and epileptic psychoses.

Cause of death	Age	1	2	3	4–5	6–10	11–25	All durations
Tuberculosis	15–29	34 6.5	38 10.8	26 10.0	42 12.6	23 7.4	2 5.4	165 9.1
	30–39	14 4.1	15 6.1	23 10.9	38 10.8	41 6.8	18 5.7	149 7.2
	40–49	7 5.8	7 8.1	4 5.2	10 7.2	14 5.2	19 5.3	56 5.8
	50–59	7 11.1	4 9.7	1 2.9	6 10.1	8 6.9	88 6.1	34 7.7
	60–69	5 9.8	2 7.2	3 13.3	2 5.2	2 2.8	7 10.2	21 7.5
	70–99	2 7.5	2 15.7	1 11.2	1 7.8	- —	3 10.0	9 7.4
	All ages	69 6.0	68 9.0	58 9.4	99 10.6	88 6.2	52 6.1	434 7.6
All other causes of death	15–29	30 5.8	5 1.5	4 1.6	3 0.9	5 1.7	- -	47 2.7
	30–39	45 8.8	14 3.8	7 2.2	15 2.8	11 1.2	10 2.1	102 3.9
	40–49	46 10.4	9 2.9	12 4.3	1 0.2	13 1.3	17 1.8	98 2.8
	50–59	56 10.2	13 3.6	13 4.4	12 2.3	9 0.9	15 1.3	118 3.1
	60–69	81 8.6	18 3.5	8 1.9	0 1.3	21 1.6	11 0.9	148 2.9
	70–99	159 7.5	25 2.6	26 3.8	15 1.7	23 1.2	23 1.1	271 3.1
	All ages	417 8.4	84 3.0	70 3.1	55 1.6	82 1.3	76 1.3	784 3.0

In table 18 an attempt is made to show the interplay of the two factors of age and duration, and in spite of the small number of cases in certain groups the trend of the table is clear. The excess mortality from tuberculosis is practically independent of age as well as of

Table 18 b. Women. Relative mortality of the insane from tuberculosis and other causes of death according to age and duration.

Cause of death	Age	1	2	3	4–5	6–10	11–25	All durations
Tuberculosis	15–29	45 12.1	26 12.6	37 24.8	31 16.0	18 10.4	3 16.1	160 14.1
	30–39	19 6.1	26 13.3	21 13.6	28 11.6	50 13.7	13 8.6	157 11.0
	40–49	11 7.5	8 8.5	14 17.9	20 15.7	31 14.2	14 9.7	98 12.1
	50–59	10 11.1	8 15.4	5 11.5	13 18.6	23 19.5	8 8.3	67 14.2
	60–69	2 3.7	5 15.4	6 23.8	2 5.4	10 15.7	6 11.5	31 11.6
	70–99	3 8.0	2 9.3	1 5.9	2 7.8	5 12.7	4 13.0	17 8.4
	All ages	90 8.7	75 12.4	84 18.0	96 13.8	137 14.0	48 9.7	530 12.4
All other causes of death	15–29	41 17.8	7 6.3	3 3.4	4 3.5	7 6.6	1 8.4	63 9.4
	30–39	71 17.8	12 4.8	2 1.0	10 4.8	21 4.5	4 2.1	120 6.6
	40–49	83 15.2	21 6.0	2 0.7	12 2.5	21 2.6	13 2.4	152 5.0
	50–59	112 14.0	28 6.0	19 4.9	14 2.2	14 1.3	17 2.0	204 4.9
	60–69	105 10.4	37 4.6	10 2.1	19 2.8	24 2.0	11 1.1	206 4.1
	70–99	125 4.7	41 2.6	19 1.6	41 2.3	33 1.3	29 1.4	288 2.4
	All ages	537 9.5	146 4.3	55 2.2	100 2.5	120 2.5	75 1.6	1033 3.9

duration. For the remaining causes of death duration is clearly the deciding factor, while age does not have any significant influence at all. Evidently the decrease of excess mortality with age is largely a statistical artefact.

The excess mortality of the insane in single and married.

It is a well known fact that in the general population the mortality is consistently higher for single persons, because the married represent a positive selection with regard to physical health—and possibly even because they lead a more protected life. We have seen that mental disease leads to a highly increased mortality, particularly during the first year of the illness. Now the problem arises: Is this effect of mental disorder upon mortality the same in the single and the married? The married patients start out as a privileged group with regard to health. Do they retain this advantage under the strain of mental illness?

When the single and the married are compared, the problem of differences in age distribution becomes even more complicated than

usual. Not only are the married considerably older than the single, but the excess mortality of the insane decreases with age (at least apparently)—and so does the excess mortality of the single, while mortality in general rises rapidly with age. The difficulties are best avoided by basing the comparison upon individual age groups only. Unfortunately Norwegian health statistics do not give the deaths by marital condition and cause of death, and we therefore have no means of singling out tuberculosis.

Table 19 gives the relative mortality of the single (S/M) in the general population and in various groups of mental patients. This makes the comparison more easy than our usual procedure of using the excess mortality of the insane. The table shows clearly that in all groups of mental patients the excess mortality of the single is lower than in the general population, and in several groups the proportion is even reversed, and mortality is highest in the married. This tendency is most marked in the male sex, it is most marked in the younger age groups, and it is less marked in schizophrenia than in the remaining diagnostic groups.

This observation seems to indicate that the influence of insanity upon physical health is so powerful that the influence of pre-psychotic factors (constitutional or environmental) is reduced to nothing.

Conclusions.

Our statistical analysis of a Norwegian material has in the main confirmed previous findings: The patients in our mental hospitals present a mortality which is from five to six times as high as that of the general population. This excess mortality is particularly high in psychoses which are accompanied by some somatic disorder, such as confusional, organic and epileptic psychoses, as well as general paresis. Among the "functional" psychoses manic-depression has a decidedly higher excess mortality than schizophrenia, while psychoses with chronic alcoholism and with constitutional psychopathic inferiority rank much lower. The excess mortality is higher in the female sex, with senile and arteriosclerotic psychoses as the only exception. Among the causes of death respiratory diseases and tuberculosis have the highest excess mortality, with infectious diseases next. Cancer is the only cause of death which is not significantly more frequent among the insane than in the general population.

While most previous investigations have dealt with entire hospital populations, the present study is based upon a material of

Table 19. Death rates per year per 10 000 of the insane and of the general population of Norway, by marital condition (S = single – M = married)

	Age	General pop. of Norway 1926–1940			Mental hospitals (first admissions), 1926–1940											
					Schizophrenia			Senile and arteriosclerotic			G.P.I. epileptic and organic			Remaining diagnoses		
		S	M	S/M	S	M	S/M	S	M	S/M	S	M	S/M	S	M	S/M
Men	25–29	58.9	24.5	2.4	236	155	1.5				714	1110	0.6	177		
	30–39	75.4	36.0	2.1	219	182	1.2				1211	1391	0.9	218	422	0.5
	40–49	101.5	51.3	2.0	176	182	1.0				952	1623	0.6	257	441	0.6
	50–59	162.1	106.2	1.5	270	281	1.0	3333	3800	0.9	1248	1920	0.7	256	571	0.4
	60–69	307.0	247.2	1.2	332	533	0.6	1615	2420	0.7	2020	2619	0.8	703	589	1.2
	70–79	685.1	618.8	1.1	606	506	1.2	2855	4340	0.7	4000	2860	1.4	889	2220	0.4
Women	25–29	44.0	31.3	1.4	392	478	0.8							564	724	0.8
	30–39	47.0	35.5	1.3	302	284	1.1				1162	1123	1.0	386	722	0.5
	40–49	62.9	48.9	1.3	291	253	1.1				1538	2197	0.7	396	715	0.6
	50–59	109.7	89.9	1.2	316	304	1.0	1446	1685	0.9	1440	2275	0.6	880	921	1.0
	60–69	220.7	201.3	1.1	554	324	1.7	1277	1800	0.7				973	1136	0.9
	70–79	524.3	573.3	0.9	673	705	1.0	2000	2145	0.9	1250	2800	0.4	1278	980	1.3

	Men	Women	Total
General paresis, cerebral syphilis	192	78	270
Epilepsy	26	22	48
Encephalitis	9	2	11
Meningitis (non epidemic), cerebral abscess.	3	12	15
Huntingtons chorea, Wilsons desease	7	4	11
Brain tumor	6	7	13
Disseminated sclerosis.	1	2	3
Others and not specified	7	9	16
Embolism etc.	7	10	17
Total no. of deaths	258	146	404

	Men	Women	Total
Cancer ventriculi	30	17	47
Cancer recti, coli	4	4	8
Cancer hepatis, pancreatis	8	10	18
Cancer uteri, urogenitalis, prostatae.	5	8	13
Cancer mammae	—	12	12
Cancer pulmonum	1	2	3
Cancer without specified location	2	5	7
Cancer of the skin	2	2	4
Sarcoma	3	1	4
Total no. of deaths	55	61	116

	Men	Women	Total
Diabetes mellitus	2	8	10
Leukemia, lymphogranulomatosis	3	2	5
Pernicious anemia	3	6	9
Pellagra	1	—	1
Basedows disease	—	4	4
Others	7	7	14
Total no. of deaths	16	27	43

	Men	Women	Total
Exhaustion, excitation	3	3	6
Delirium acutum	—	3	3
Inanition	7	4	11
Insanity, schizophrenia etc.	9	33	42
Paralysis cordis	21	19	40
Mors subita	8	8	16
Kachexia, marasmus, debilitas (not specified as senile)	11	23	34
No cause of death given	4	5	9
Total no. of deaths	63	98	161

	Men	Women	Total
Bronchopneumonia	139	168	407
Lobar pneumonia	48	52	100
Hypostatic pneumonia	2	6	8
Pneumonia, not specified	31	37	68
Bronchitis	7	11	18
Empyema, pulmonary abscess	8	9	17
Pulmonary gangrena	7	3	10
Others and not specified	5	2	7
Total no. of deaths	247	288	535

	Men	Women	Total
Sepsis, pyemia, phlegmone, abscessus	28	28	56
Acute infectious gastro-enteritis	10	20	30
Erysipelas	6	8	14
Influenza, febris catharrhalis	12	7	19
Rheumatismus acutus	1	—	1
Typhoid	—	2	2
Meningitis (pnemococcic)	—	1	1
Diphteria	1	—	1
Tetanus		1	1
Parotitis epidemica	1	—	1
Malaria (therapeutic)	2	—	2
Acquired syphilis	1	—	1
Total no. of deaths	62	67	129

	Men	Women	Total
Vitium org. cordis, endocarditis chronica	46	51	97
Myocarditis chronica	27	39	66
Ruptura cordis et aortae	3	2	5
Embolia, thrombo-phlebitis	4	12	16
Aortitis, aneurysma aortae	3	1	4
Others	2	9	11
Total no. of deaths	85	114	199

	Men	Women	Total
Chronic nephritis	19	25	44
Acute nephritis	1	4	5
Cysto-pyelitis, pyo-nephritis	12	15	27
Lithiasis renis	2	—	2
Prostatic hypertrophy	1	—	1
Sectio caesarea	—	1	1
Others and not specified	2	1	3
Total no. of deaths	37	46	83

	Men	Women	Total
Chronic entero-colitis	12	34	46
Ileus, hernia incarcerata	16	19	35
Peritonitis	4	9	13
Acute appendicitis	3	1	4
Ulcus ventriculi et duodeni	12	2	14
Parotitis non epidemica	2	3	5
Diseases of liver and gall bladder	2	4	6
Necrosis of the pancreas	3	1	4
Others and unspecified	3	4	7
Total no. of deaths	57	77	134

first admissions only, which is particularly suited for a detailed analysis of the influence upon excess mortality of the duration of the hospital stay. Our findings show that this factor is of decisive importance. In all types of mental disorder and in all age groups the excess mortality has its maximum during the first year following admission, and it decreases markedly from year to year. In view of this observation certain findings concerning the mortality of mental patients must be regarded as misleading and in need of revision.

1. A population of mental hospital patients includes a number of chronics and convalescents with a comparatively low excess mortality. Such a mixed material does therefore not give an adequate picture of the tremendous influence of active mental illness upon mortality.

2. In the acute stages the excess mortality is much higher in manic-depressive psychosis than in schizophrenia—a fact which is easily covered up when duration is disregarded.

3. The apparent decrease of excess mortality with age is largely a statistical artefact, caused by: a) the prevalence of chronic cases in the higher age groups, and b) the prevalence in higher age groups of diseases which do not show a very high excess mortality among the insane.

Some practical and theoretical implications of our findings for psychiatry in general will be discussed in a forthcoming publication.

Summary.

A study of 21,522 first admissions to Norwegian mental hospitals has confirmed the previous findings of a very high excess mortality in these patients, particularly from tuberculosis, respiratory and in-

fectious diseases. It is shown that this excess mortality is highest during the first year of hospitalization, while chronic patients tend towards a normal mortality. Tuberculosis forms an exception, with a uniformly high excess mortality, independently of age and duration. For the remaining causes of death the duration of the psychosis is the decisive factor, which therefore has to be kept constant whenever groups of mental patients (diagnostic or other) are to be compared. If this is disregarded, statistical artefacts tend to arise, such as the apparent decrease of excess mortality with age.

Résumé.

Etudiant les 21522 premières admissions dans les hôpitaux psychiatriques norvégiens, l'auteur confirme qu'il existe chez ces malades un taux excessivement élevé de mortalité, due spécialement à la tuberculose et aux affections respiratoires et infectieuses, ce qui avait déjà été signalé antérieurement. Cet excès de mortalité est particulièrement marqué au cours de la première année d'hospitalisation, les malades chroniques tendant à avoir un taux de mortalité normal. La tuberculose constitue cependant une exception, la mortalité restant uniformément trop élevée, indépendamment de l'âge et de la durée de la maladie. La durée de l'affection psychiatrique constitue dans toutes les autres causes de mort le facteur décisif. Ce dernier doit donc être pris comme une constante importante toutes les fois que l'on compare des groupes de malades mentaux, au point de vue du diagnostic ou à tout autre point de vue. Si ce n'est pas le cas, on introduit des causes d'erreur statistiques qui conduisent à des conclusions erronnées, telle la diminution apparente de l'excès de mortalité avec l'âge.

Zusammenfassung.

Eine Untersuchung von 21 522 Patienten, welche zum ersten Male in ein norwegisches Geisteskrankenhaus eingeliefert wurden, hat eine schon früher entdeckte, stark erhöhte Sterblichkeit bei diesen Patienten bestätigt, verursacht vor allem durch Tuberkulose, Krankheiten der Atmungsorgane und Infektionskrankheiten. Es zeigt sich, daß diese erhöhte Sterblichkeit ihren Höhepunkt im ersten Jahre des Aufenthaltes im Krankenhause erreicht, während kronische Patienten einer annähernd normalen Sterblichkeit unterliegen. Eine Ausnahme bildet die Tuberkulose mit einer unverändert überhöhten Sterblichkeit, unabhängig von Alter und Krankheitsdauer. Den ent-

scheidenden Faktor für die übrigen Todesursachen bildet die Dauer der Geisteskrankheit, welche deshalb eine wichtige Konstante ausmacht, wenn Gruppen von Geisteskranken miteinander verglichen werden, sei es im Hinblick auf eine Diagnose oder unter anderen Gesichtspunkten. Wird dies übersehen, so entstehen statistische Fehlerquellen, welche zu falschen Schlußfolgerungen führen, wie ein scheinbares Abnehmen der erhöhten Sterblichkeit mit dem Alter.

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A NOTE ON THE RELATIVE DEATH RATE

by GUNNAR DAHLBERG, M.D.

If we were the fortunate possessors of a much better memory and a more God-like intelligence, we would never have to apply statistical methods to numerical material. We would be able to keep in our minds all the separate values in a series of numbers and to compare directly two or more such series. Our mental equipment being as it is, we must use statistics and try to obtain simple figures from which conclusions can be drawn. It is for this reason that statistics is an essential tool that to some extent enables us to compensate for our sadly inadequate intelligence. Only after statistical treatment can we draw definite conclusions, in the drawing of which due regard has been paid also to random variation.

For comparing the mortalities in two groups one may use the quotients between the actual mortality in the groups and the one that is normal for the population. Such quotients provide an indication of how much higher or lower the group mortality is. Naturally, if the quotient is unity the mortalities are equal. However, the situation is complicated by the fact that in a population the mortality is not the same at all age levels. One must therefore compute special quotients for different age groups; and these must not be too broad, i.e. must not embrace too many years. Even so, however, it is not always a satisfactory method to compare quotients.

I shall demonstrate this by taking mental patients as an example. The mortality of the insane exceeds that of the normal population, which has been shown by *Malzberg*, *Ödegård* and *Alström*. However, to show the relative excess mortality these authors have consistently used the quotient between two mortalities (excess mortality rate) and in certain respects arrived at misleading figures. For example, if a mental hospital is bombed in wartime and as a result 6 $^0/_{00}$ of the patients are killed, then this mortality will be distributed equally among old and young persons. Let us assume that the mortality is 3 $^0/_{00}$ at age 18 and that it therefore rises to 9 $^0/_{00}$. (The figures for normal populations are taken from Swedish vital statistics from 1936–1940.) For this age group the relative death rate consequently is 3. For 60 years old women in the normal population the death rate is 15 $^0/_{00}$, and by assumption this death rate rises to 21 $^0/_{00}$. The resultant relative death rate will be $\frac{21}{15}$, i. e. 1.4. This is evidently much less than the relative death rate at age 18, despite the assumed equal excess death rate due to bombing. This is in other words an instance when the relative death rates are in some respects misleading. Similarly, if owing to tuberculosis, infectious hepatitis, or some other infectious disease the mortality is affected to approximately the same extent at different ages, the relative death rates are unsuitable to prove this. In such cases it is more correct to use the difference between the normal and the excess death rate in the group. Only by this means can it be shown that the risk increase is equal at the different age levels. It would, from this point of view, be advisable to publish both the difference from the normal death rate and the relative death rate, and then discuss the figures from different aspects. The conclusion should not be drawn from the above that it is wrong to use relative death rates, I merely wish to illustrate that they incompletely depict the mortality problem.

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A NOTE ON THE THROMBOCYTES IN HEMOPHILICS

by ANDERS PARROW

For quite a long time it has been known that in hemophilics the blood constituents are fully normal, in so far as the blood sooner or later coagulates. It has been established that hemophilia is due to a hereditary factor, but the exact mechanism causing the reduced coagulability is still discussed. A proposed cause agent has, for instance, been the absence of an antihemophilic plasma factor that is present in normal blood. A change in the thrombocytes, reducing their effect, has also been suspected, but no abnormal morphologic change has so far been proved. It would seem to be justified, however, to investigate the problem once more with the use of new methods, which are more exact and reliable than earlier ones.

In so doing I used a method developed by Fonio for darkfield thrombocyte microscopy. To two parts of venous blood are added seven parts by volume of a 14 per cent solution of $MgSO_4$. The mixture is centrifuged for seven minutes at 2000 r.p.m. The supernatant, which contains no erythrocytes, is saved. The $MgSO_4$ solution serves as an anticoagulant. To ensure that the blood shall contain as few fat-drops as possible, it is important to take the blood sample in the morning before the test person has eaten. By this means Fonio has taken unusually good photographs of the thrombocytes in normal blood. Apparently, though, he has not examined the thrombocytes in hemophilics.

All the various transformations of the thrombocytes before they finally disintegrate are beautifully seen under the microscope. For the purpose at hand it was particularly interesting to study the pseudopodia which according to Fonio-Schwendener (Die Thrombozyten des menschlichen Blutes, 1942) play such an important part in the clotting process. The authors maintained that the coagulation

commences when the thrombocytes disintegrate, the thrombokinase in them being set free in the plasma. As a rule the disintegration of the thrombocytes seems to start only after they, with the aid of the pseudopodia, have attached themselves to the uneven surface offered by, for instance, a glass receptacle or a damaged blood vessel. This being so, it might be expected that in hemophilics the thrombocytes have no pseudopodia, or that the pseudopodia are different, or that fewer thrombocytes have pseudopodia. No evidence in support of the first two assumptions could be observed. The thrombocytes from the hemophilic that I examined (coagulation time: 2 h 10 m) so far as could be seen showed the same picture as thrombocytes from normal blood and developed in the same manner before disintegrating, without in any way differing from normal thrombocytes.

The question whether fewer thrombocytes have pseudopodia is not so easy to answer. It must be kept in mind that the thrombocytes are present in different forms, by Fonio termed Ruhe-, Reiz- and Übergangsform. The thrombocytes in the blood occur also in a form without pseudopodia, which form may be transformed quickly either directly to Reizform or to Ruheform. From Reizform the thrombocyte may be converted either via Übergangsform to Ruheform or it may disintegrate. (Also the Ruheform in time disintegrates after it has stuck to the slide.) Owing to this variety of forms one never sees only thrombocytes with pseudopodia but always a mixture of thrombocytes with and without pseudopodia. The majority, however, have pseudopodia, and as soon as 20–25 minutes after venipuncture most of the thrombocytes have pseudopodia. Whether or not the inactive form of thrombocytes seen in the bloodstream of hemophilics is less quickly transformed into the active Reizform seen in the slide is at present impossible to say. The reason is that from the venipuncture to the dark-field picture 20–25 minutes elapse and the assumedly slower hemophilic thrombocytes may by then have caught up with the assumedly faster normal thrombocytes.

I consider it justified to publish this negative result. Also such results are interesting, and this one may save later investigators some trouble, for the adopted method does not lead to the desired result.

In conclusion I wish to thank the State Institute of Human Genetics and Race Biology and Docent *Eric Sköld*, M.D., for having helped me to obtain a test person. In addition I wish to express my gratitude to Professor *Martin Wrete*, M.D., for letting me use the resources of his Institute and its laboratories.

SEASONAL BIRTH FREQUENCIES IN PARAMETERS

by H. J. STUTVOET, Amsterdam

Introduction.

It is generally known that the number of births of children shows seasonal fluctuations. The causes are manifold. They may be of biological, psychological and social nature. In primitive times biological causes will have been the most important, if not the only ones. As with animals birth generally occurs in the time most favourable for the newborns and thus for the maintenance of the species, it is to be expected that this also holds good with regard to man. In the course of human evolution and due to increasing civilization psychological and social factors certainly have obtained a greater influence.

On account of the biological causes it may be expected that the number of human births in the different parts of the year will be strongly influenced by the climate and the seasons. As seasons return periodically, periods in the birth frequencies of man can also be expected.

When we distribute the number of births of any population over the calendar months and make a polygon of these frequencies, then this polygon shows two peaks besides smaller ups and downs. Of course this distribution is subject to the different duration of the months, but after elimination of this factor the two peaks mostly remain. Often the occurrence of two peaks in a frequency diagram points to heterogeneousness of the underlying statistical material. Subdivision of the material into two more homogeneous groups may give rise to two unimodal frequency distributions. In studying human birth frequencies one cannot a priori state the existence of two more homogeneous groups; when we have analyzed the general frequency-diagram into two one-peak-polygons, they must be considered to have a purely descriptive nature and one must not ascribe any aetiological significance to them.

The possibility remains that a subdivision of an originally purely descriptive significance may lead to the discovery of the causes explaining the occurrence of the two peaks in the frequency-diagram.

This can only be done with the aid of experts in the field to which the material concerned refers.

The choice of the frequency curve.

The illustrations in which the frequencies are presented scarcely give possibilities for exact comparison. Therefore we try to express the distributions in another way. This can be realised if we look for special norms or characteristics. Such numbers or parameters then represent the distribution in some way. For that purpose we try to find the mathematical equation of a curve fitting the frequency-diagram as well as possible. This "as well as possible" is generally interpreted in such a way that the sum of squares of the differences between the frequency-diagram and the frequency-curve is a minimum. As we expect periodicity in the distribution of birth frequencies, the choice of a frequency-curve falls on the sinusoïde ($y = A \sin x$). This curve, however, shows one maximum per period (fig. 1 a). The curve with equation $y = B \sin 2x$ has two maxima per period (fig. 1 b). Each separate curve has too great a regularity to express the fluctuations of a birth frequency curve. But a synthesis of both curves—especially when we give each some phase-displacement—gives a picture that is quite similar to that of the birth frequency-diagrams (fig. 1 c). In this manner we have decomposed the annual period in birth frequency curves into two periods or rhythms. These rhythms have only a descriptive value. When composed they give rise to a curve which can be expressed by the equation

$$y = A \sin (x + \alpha) + B \sin 2 (x + \beta).$$

This curve has 4 parameters: A, B, α and β, which thus can be used as norms in comparing two birth frequency curves.

It is possible to obtain curves, which will perhaps fit the given frequency-diagram even better, but then the number of parameters will increase and the method loses its practical usefulness. Indeed we cannot study statistics for its own sake, but we must claim that the employed method is surveyable.

The method to be used by us requires considerably more work than usual, but this disadvantage is amply compensated by the advantage that the comparison of the collectives can be executed more exactly.

Determination of the frequency-curve.

The mathematical basis for the method of computation used here to determine the frequency-curve fitting to a given frequency-

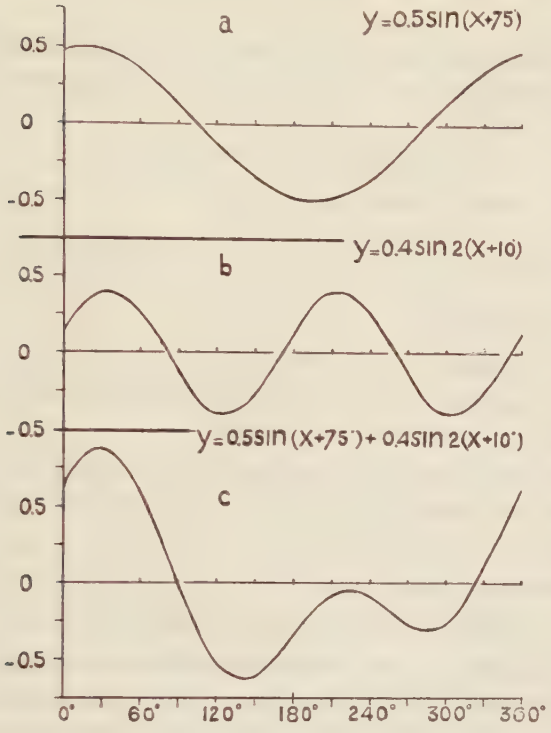

Fig. 1.

polygon will be dealt with at the end of this paper. Here we shall only give the computation.

We have at our disposal the monthly numbers of births. As these months are not of equal duration we must first make a correction. For this purpose we generally use the birth rates, which can be obtained from the following formula:

$$\text{rate} = \frac{\text{No. of births in month}}{\text{No. of births in year}} \times \frac{\text{No. of days in year}}{\text{No. of days in month}} 1.00.$$

It is obvious that the sum of the rates is about 1.200.

In order to obtain the monthly birth percentages (of the corrected months) the rate of each month must be divided by 12. These percentages show deviations with regard to the mean percentage, which of course amounts to 8.33.

On the X-axis Jan., Febr., etc. correspond with the values $x = 0^0, 30^0, 60^0, \ldots 330^0$ respectively. In the direction of the Y-axis

we measure the deviation of each monthly birth percentage from the mean 8.33. In order to obtain the equation of the curve fitting to these points, viz.

$$y = A \sin (x + \alpha) + B \sin 2 (x + \beta)$$

we compute α and β from resp.

$$\text{tg } \alpha = \frac{\Sigma\, y \cos x}{\Sigma\, y \sin x} \text{ and } \text{tg } 2\,\beta = \frac{\Sigma\, y \cos 2x}{\Sigma\, y \sin 2x}$$

and then A and B from

$$A = {}^1/_6\, \Sigma\, y \sin (x + \alpha); \quad B = {}^1/_6\, \Sigma\, y \sin 2 (x + \beta).$$

The four parameters A, B, α and β determine the behaviour of the fluctuations sufficiently and simply.

For instance we take the numbers of live births in The Netherlands during the years 1932–1939 in the communities of less than 5.000 inh.

The computed percentages are

$$8.33 + A \sin (x + \alpha) + B \sin 2 (x + \beta).$$

Now we calculate the correlation between the computed and observed percentages. The coefficient of correlation amounts to $r = 0.9790 \pm 0.0119$. The resemblance of the observed polygon and the computed curve is striking.

No. of month	x	%	y	y x cos x	y x sin x	y cos 2x	y sin 2x	sin (x + α)	y sin (x + α)	sin 2 (x + β)	y sin 2 (x + β)
1	0°	8.36	0.03	0.03	0.	0.03	0.	0.126	0.00	—0.041	0.00
2	30°	.9.04	0.71	0.61	0.35	0.35	0.61	0.605	0.43	0.845	0.60
3	60°	9.04	0.71	0.35	0.61	—0.35	0.61	0.922	0.65	0.886	0.63
4	90°	8.67	0.34	0.00	0.34	—0.34	0.	0.992	0.34	0.041	0.01
5	120°	8.49	0.16	—0.08	0.14	—0.08	—0.14	0.796	0.13	—0.845	—0.14
6	150°	8.17	—0.16	0.14	—0.08	—0.08	0.14	0.387	—0.06	—0.886	0.14
7	180°	8.30	—0.03	0.03	0.	—0.03	0.	—0.126	0.00	—0.041	0.00
8	210°	8.29	—0.04	0.03	0.02	—0.02	—0.03	—0.605	0.02	0.845	—0.03
9	240°	8.31	—0.02	0.01	0.02	0.01	—0.02	—0.922	0.02	0.886	—0.02
10	270°	7.96	—0.37	0.	0.37	0.37	0.	—0.992	0.37	0.041	—0.01
11	300°	7.68	—0.65	—0.32	0.56	0.32	0.56	—0.796	0.52	—0.845	0.55
12	330°	7.79	—0.54	—0.47	0.27	—0.27	0.47	—0.387	0.21	—0.886	0.48
				0.33	2.60	—0.09	2.20		2.63		2.21

$$\text{tg } \alpha = \frac{33}{260} = 0{,}127 \qquad \text{tg } 2\beta = \frac{9}{220} \qquad A = \frac{2.63}{6} = 0.44 \qquad B = \frac{2.21}{6} = 0.37$$

$$\alpha = 7^0\ 14' \qquad 2\beta = -2^0\ 21'$$

Hence we obtain the following table:

No. of month	Computed percent.	Observed percent.
1	8.37	8.36
2	8.91	9.04
3	9.07	9.04
4	8.79	8.67
5	8.37	8.49
6	8.17	8.17
7	8.25	8.30
8	8.37	8.29
9	8.25	8.31
10	7.91	7.96
11	7.67	7.68
12	7.83	7.79

In fig. 2a we find both the polygon and the curve; in fig. 2b the computed curve is dissolved into its two components:

$$y_1 = 0.44 \sin (x + 7^0) \quad \text{and} \quad y_2 = 0.37 \sin 2 (x - 1^0),$$

α and β being rounded off to degrees.

We shall call the first curve the A-rhythm, characterized by its amplitude $A = 0.44$ and its phase $\alpha = 7^0$. Analogously the B-rhythm is characterized by its amplitude $B = 0.37$ and its phase $\beta = -1^0$. A superficial consideration of fig. 2 shows already that, α and β being nearly equal and small, the high birth frequency in

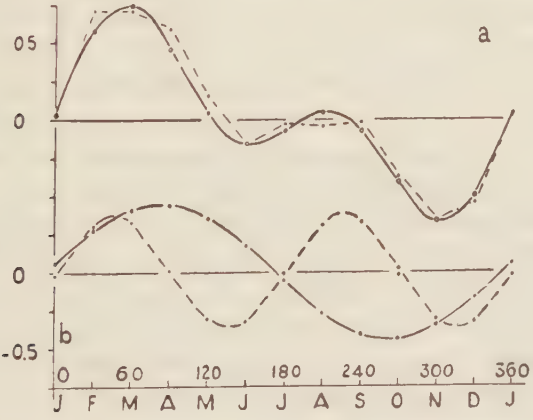

Fig. 2. Monthly live births in percentages in The Netherlands 1932–'39.

Febr.–March is the effect of the cooperation of the amplitudes A and B. Analogously the low birth frequency in Oct.–Nov. can be explained. A second faint peak may arise in Aug. or Sept. depending on the values of A, B, α and β.

A closer consideration of the equation of the curve shows that the intersections with the X-axis are found from $\sin(x + \alpha) = 0$ and $\sin 2(x + \beta) = 0$ or

$x + \alpha = 0^0, 180^0, 360^0$ and $x + \beta = 0^0, 90^0, 180^0, 270^0, 360^0$.

When two intersections of the A- and B-curve coincide, we can distinguish 4 cases:

1. $\alpha - \beta = 0^0$. The two curves ascend both from the same intersection. If $A > B$, then the total curve rises very sharply to its maximum, descends further slowly to its minimum followed by a sharp rise again (fig. 3a and 3c).

2. $\alpha - \beta = 0^0$. If however $A < B$, then the curve reaches a maximum, followed by a secondary minimum, a secondary maximum and a strongly marked minimum respectively, when we start at the common intersection from which both curves ascended (fig. 5d, Birth frequency curve of U.S.A.-South, 1933–'40).

3. $\alpha - \beta = 90^0$. From one of the intersections on the X-axis the A-curve ascends and the B-curve descends. If $A > B$, then the total curve rises slowly to its maximum and after that descends sharply to its minimum (fig. 5b, Birth frequency curve of U.S.A.-West 1933–'40).

4. $\alpha - \beta = 90^0$. If however $A < B$, then we see respectively a secondary minimum, a high maximum, a deep minimum followed by a secondary maximum (fig. 6, Birth frequency curve of U.S.A. 1933–'40).

Usefulness of the four parameters to compare birth frequency curves.

We will give some examples to demonstrate the usefulness of the four parameters in comparing birth frequency curves.

As a first example we choose the birth frequency curves of Switzerland during the decennaries: 1871–'80, 1881–'90, 1891–'00, 1901–'10, 1921–'30 and 1931–'40. The data are taken from *von Steiger* (1)[1]). The live birth rates of *von Steiger* have been reduced to percentages and after that for each decennary the parameters A, B, α and β have been computed.

[1]) The figures in brackets refer to the list of literature.

In order to check the correspondence between the frequency curves and the polygons given by the data, we have computed the coefficients of correlation between the observed and the computed percentages. These are so large that we can consider the curves as very good representatives of the polygons.

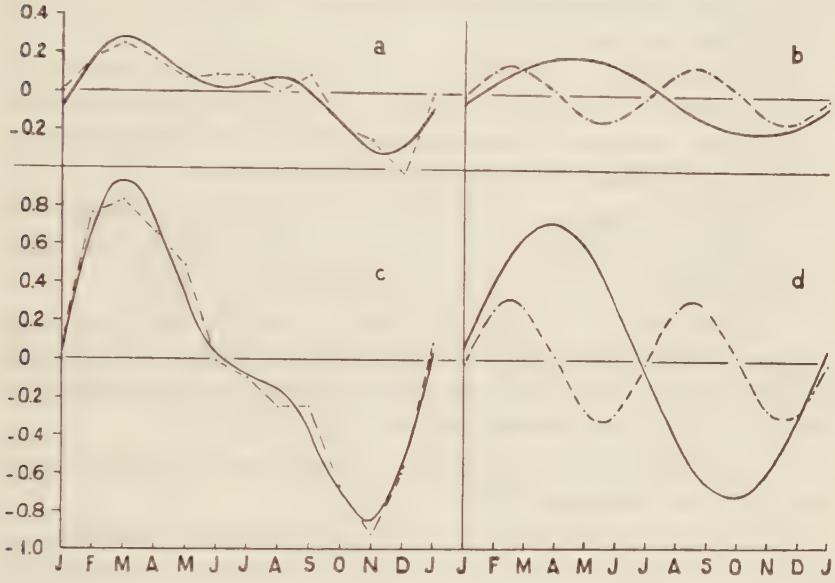

Fig. 3. Monthly live births in percentages in Switzerland, a and b: decennary 1871–'80; c and d: decennary 1931–'40.

In fig. 3a the polygon for 1871–'80 is drawn together with the curve. In fig. 3b the curve is decomposed into its two rhythms. Fig. 3c and 3d represent the corresponding curves for the decennary 1931–'40. The computed parameters and coefficients of correlation are summarized in the following table:

Live Births in Switzerland

Decennary	A	B	α	β	Coeff. of corr. between comp. and observ. perc.
1871–'80	0.20	0.15	—17	—3	0.9328 ± 0.0375
1881–'90	0.23	0.19	0	9	0.9721 ± 0.0158
1891–'00	0.31	0.21	—28	—6	0.9845 ± 0.0045
1901–'10	0.40	0.29	—23	—7	0.9763 ± 0.0069
.....	....	....	....	...	.....
1921–'30	0.69	0.27	3	1	0.9905 ± 0.0027
1931–'40	0.72	0.32	5	—2	0.9889 ± 0.0034

Hence we see that in the course of 70 years the amplitude A increased continually. The same can be said of B (with a single interruption). B however does not increase to the same extent as A. Therefore the second peak of Aug.-Sept. disappears. The births are concentrated more round about the maximum and the minimum. The cause of this phenomenon must be discovered eventually by students in medicine and sociology.

We can imagine that by better medical knowledge and evolution of chemical science the possibilities of conception are increased so that the conscious or unconscious preference of the parents for the time of birth is expressed more clearly.

A very large number of our birth frequency computations have revealed that the differences in rural and urban population also have a great influence on the values of the parameters.

As the course of A and B show a great similarity we may suppose that if A and B depend on certain causes. these causes might be the same for A and B. The coefficient of correlation between A and B for the 6 decennaries amounts to 0.857 ± 0.109.

A second important fact we state is the small fluctuation of α and the great constancy of β.

Each degree corresponding with about one day, the intersections of the two rhythms with the X-axis both fall nearly on the 1st of January. The maximum of the A-rhythm is hence situated in the first half of March and the conception time in the beginning of December. The two maxima of the B-rhythm are situated in the second halves of Febr. and Aug. and the conception times in the second halves of Nov. and May.

The abnormal period of World War II interrupts the regular increase of A and B, but does not influence α and β. In the post war years A and B restore themselves and try to follow the original course. This is shown in the following table.

Period	A	B	α	β	coeff. of corr.
1941–'47	0.63	0.19	1	—12	0.9905 ± 0.0054
1945	0.64	0.30	15	—11	0.9577 ± 0.0239
1946	0.90	0.32	4	1	0.9692 ± 0.0175
1947	0.87	0.23	4	— 2	0.9929 ± 0.0041
1948	0.88	0.32	11	1	0.9037 ± 0.0558

As a second example we choose the data of *Bickel* (2) about the still births in Switzerland.

Bickel compares the numbers of live births and still births per month during the periods 1932–'40 and 1941–'47 and concludes that the rhythm of the still births is displaced one month because there are very many premature births among the still births. However, he speaks of an increase of the number of still births in October, which he cannot explain.

When we denote the rhythms of live and still births in parameters we find during 1932–'40:

Switzerland 1932–'40		A	B	α	β	coeff. of correlation
Fig. 4a	Live births	0.71	0.31	3	—4	0.9889 ± 0.0034
Fig. 4b	Still births	0.82	0.23	38	2	0.9450 ± 0.0309

Now a comparison is possible. The most important difference between live and still births appears in the value of α. The A-rhythm

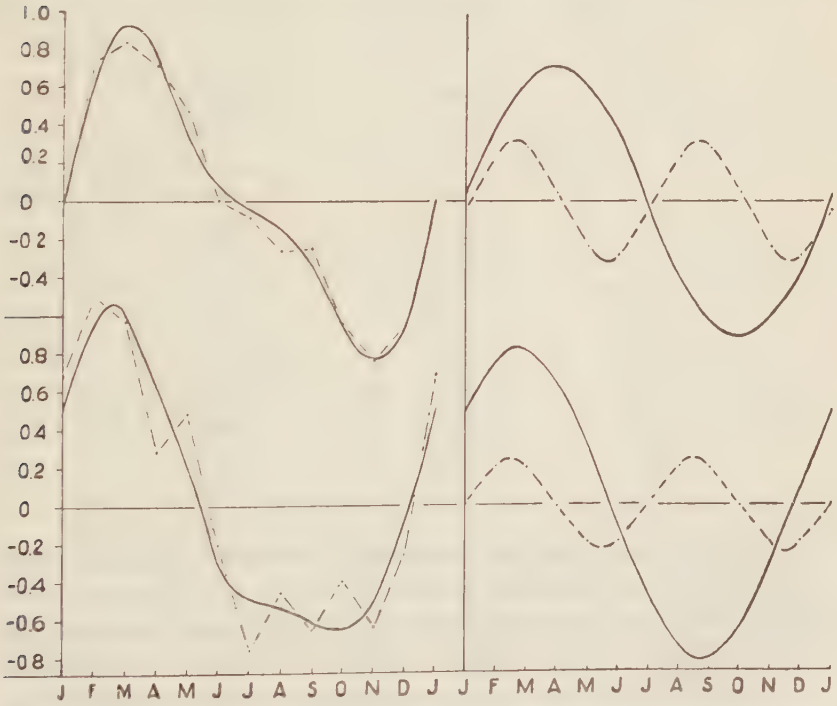

Fig. 4. Monthly live and still births in percentages in Switzerland, 1932–'40.

indeed is displaced 35 days, pointing to the cause given by *Bickel*. However, no change of importance appears in β.

The polygon of the still births shows some irregularities, probably because the numbers of still births are much smaller than those of the live births. In the curve the irregularities and accidental disturbances are smoothed out.

If we want to compare the rhythm of the still births with that of the live births, we must determine a curve characterized by the A and B of the still births and the α and β of the live births. This indeed implies a correction with respect to the fact that the still births are mainly premature births. Now we find a corrected curve of the still births.

The live births rates are

$$12 \left\{8.33 + 0.71 \sin (x + 3^0) + 0.31 \sin 2 (x - 4^0)\right\}$$

and the corrected rates for the still births are

$$12 \left\{8.33 + 0.82 \sin (x + 3^0) + 0.23 \sin 2 (x - 4^0)\right\}.$$

Hence

No. of month	Monthly rates 1932–1940	
	live births	still births corrected
1	99.9	100.1
2	107.6	107.4
3	110.0	111.3
4	109.1	110.1
5	104.2	106.0
6	101.0	101.9
7	98.9	99.2
8	98.2	96.9
9	95.9	93.8
10	92.1	90.6
11	90.0	89.7
12	92.1	93.0

It can be concluded that an increase in the number of still births during October is out of the question. It is striking, however, that the still births rates are only smaller than the live births rates in the months August-November (when we neglect Febr.).

Like *Bickel* we have made an analogous computation for the period 1941–'47. The parameters are

1941–1947	A	B	α	β
Live births	0.63	0.19	1	—12
Still births	0.70	0.38	44	4

Again, the most important difference is found in the values of α. This might indicate that the still births are nearly 1½ month too early. But as 1941–'47 is an abnormal period, we will not attach too great a significance to these data. We should have to repeat the calculations for some normal decennaries to see if the significant difference in α and the difference in seasonal influence on live and still births will be maintained.

As a third illustration of the use of the parameters A, B, α and β in comparing birth frequencies we take the birth curves of several different parts of the U.S.A.

Evelyn Halpin and *Shapiro* (3) computed a seasonal index to express the monthly variations in the crude birth rate over the period 1933–'40. The sum of these indices is 1.200. We have transposed every month index as a percentage of the sum of the indices to make the comparison with former computations possible.

A fitting curve has been computed for every polygon, showing the course of the seasonal index. A coefficient of correlation was calculated as a measure for "goodness of fit". The results are as follows (fig. 5):

U.S.A. 1933–'40	A	α	B	β	coeff. of corr.
North East	0.34	—67	0.26	18	0.9654 ± 0.0196
West	0.32	—83	0.15	13	0.9966 ± 0.0019
North Central	0.22	—98	0.35	14	0.9799 ± 0.0114
South	0.13	—167	0.52	6	0.9793 ± 0.0118
U.S.A. total	0.17	—89	0.36	9	0.9845 ± 0.0089

We have arranged the different parts of the U.S.A. according the decreasing values of A. The table shows very clearly that α is also decreasing constantly, β is almost constant but demonstrates a tendency to decreasing, while B shows an increase besides one single interruption.

It is a pity the authors have not given a further differentiation of the material. Otherwise it would have been brought to light more

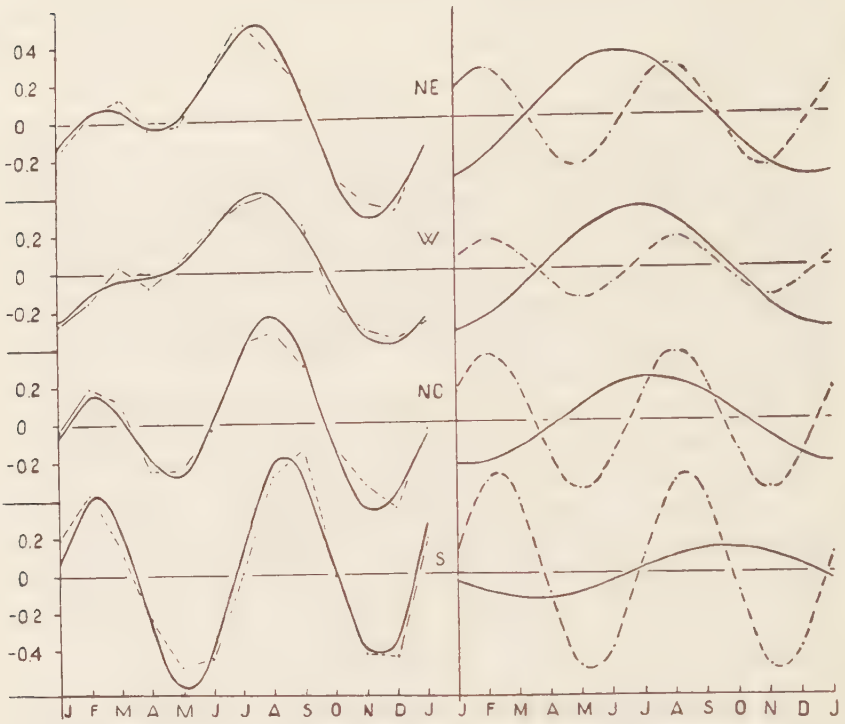

Fig. 5. Monthly live births in percentages in several parts of the U.S.A. 1933–'40; NE = North East; W = West; NC = North Central; S = South.

clearly how the four parameters are influenced by contrasts in climate, agriculture and industry, and level of culture.

The authors have also examined the possible change in the seasonal index by comparing the period 1922–'29 with 1933–'40.

Instead of drawing conclusions from their two tables it seems preferable to use the parameters. If the change is a fact, this must be sought mainly in a little displacement of the nodes.

	A	α	B	β	coeff. of correlation
A part of the U. S. A.					
1922—' 29	0.25	—51	0.29	5	0.9833 ± 0.0096
The same part					
1933—' 40	0.25	—66	0.26	15	0.9779 ± 0.0126

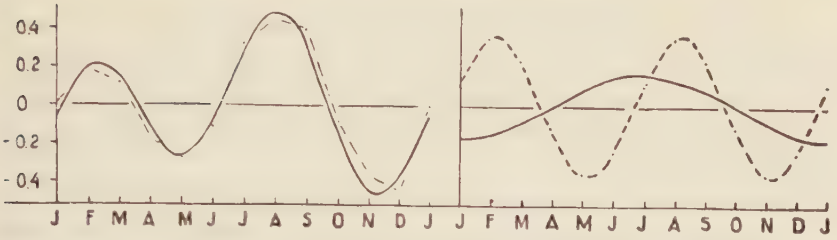

Fig. 6. Monthly live births in percentages in the U.S.A. 1933–'40.

Mathematical treatment of the problem.

To express the periodicity of the birth rhythm we have chosen the curve: $y = A \sin (x + \alpha) + B \sin 2 (x + \beta)$.

There remains only to be examined how the constants of this curve are computed from the data. At an arbitrary value of x, for instance x_i, the observation gives a value y_i and the proposed curve a value

$$y = A \sin (x_i + \alpha) + B \sin 2 (x_i + \beta).$$

We made the condition to the curve that $\Sigma (y_i - y)^2$ should be a minimum.

We denote $\Sigma (y_i - y)^2$ by P, hence

$$P = \Sigma \{y_i - A \sin (x_i + \alpha) - B \sin 2 (x_i + \beta)\}^2.$$

If P is to be a minimum, then the following conditions must be fulfilled:

$$\frac{\delta P}{\delta A} = 0; \quad \frac{\delta P}{\delta B} = 0; \quad \frac{\delta P}{\delta \alpha} = 0; \quad \frac{\delta P}{\delta \beta} = 0.$$

These conditions can be denoted also as:

$$\Sigma \{y_i - A \sin (x_i + \alpha) - B \sin 2 (x_i + \beta)\} \sin (x_i + \alpha) = 0$$
$$\Sigma \{y_i - A \sin (x_i + \alpha) - B \sin 2 (x_i + \beta)\} \sin 2 (x_i + \beta) = 0$$
$$\Sigma \{y_i - A \sin (x_i + \alpha) - B \sin 2 (x_i + \beta)\} \cos (x_i + \alpha) = 0$$
$$\Sigma \{y_i - A \sin (x_i + \alpha) - B \sin 2 (x_i + \beta)\} \cos 2 (x_i + \beta) = 0$$

The symbol Σ denotes here and further on a summation extending over the 12 values: $x_i = 0^0, 30^0, 60^0, \ldots 330^0$,
so that $\Sigma \sin x_i = 0$, $\Sigma \cos x_i = 0$, $\Sigma \sin 2x_i = 0$, $\Sigma \cos 2x_i = 0$, $\Sigma \sin^3 x_i = 0$, $\Sigma \cos^3 x_i = 0$.

It is obvious, that also

$\Sigma \sin (x_i + \alpha)$, $\Sigma \cos (x_i + \alpha)$, $\Sigma \sin^3 (x_i + \alpha)$, $\Sigma \cos^3 (x_i + \alpha)$, $\Sigma \sin 2 (x_i + \alpha)$, $\Sigma \cos 2 (x_i + \alpha)$ and $\Sigma \cos 4 (x_i + \alpha)$ all are zero.

Hence we find for instance, that

$\Sigma \cos x_i \sin 2 x_i = 2 \Sigma \cos^2 x_i \sin x_i = 2 \Sigma \sin x_i - 2 \Sigma \sin^3 x_i = 0$

and on a similar manner

$\Sigma \cos x_i \cos 2 x_i$, $\Sigma \sin x_i \sin 2 x_i$ and $\Sigma \sin x_i \cos 2 x_i$ all are zero.

Now it is possible to express $\Sigma \sin 2 (x_i + \beta) \sin (x_i + \alpha)$ in the forms mentioned above, so that this sum is zero too.

The same will hold for

$\Sigma \sin 2 (x_i + \beta) \cos (x_i + \alpha)$ and $\Sigma \cos 2 (x_i + \beta) \sin (x_i + \alpha)$.

The form $\Sigma \sin^2 (x_i + \alpha) = \frac{1}{2} \Sigma \{1 - \cos 2 (x_i + \alpha)\} = 6$ and

$\Sigma \sin^2 2 (x_i + \beta) = \frac{1}{2} \Sigma \{1 - \cos 4 (x_i + \beta)\} = 6$

The conditions on which P will be a minimum can now be reduced to

$$\Sigma y_i \sin (x_i + \alpha) - 6A = 0 \quad \text{(i)}$$
$$\Sigma y_i \sin 2 (x_i + \beta) - 6B = 0 \quad \text{(ii)}$$
$$\Sigma y_i \cos (x_i + \alpha) = 0 \quad \text{(iii)}$$
$$\Sigma y_i \cos 2 (x_i + \beta) = 0 \quad \text{(iiii)}.$$

Condition (iii) is to be expressed as follows:

$\Sigma y_i (\cos x_i \cos \alpha - \sin x_i \sin \alpha) = \cos \alpha \Sigma y_i \cos x_i - \sin \alpha \Sigma y_i \sin x_i = 0$ hence

$$\operatorname{tg} \alpha = \frac{\Sigma y_i \cos x_i}{\Sigma y_i \sin x_i}.$$

Similarly (iiii) gives

$$\operatorname{tg} 2 \beta = \frac{\Sigma y_i \cos 2 x_i}{\Sigma y_i \sin 2 x_i}.$$

After the computation of α and β (i) and (ii) give

$A = \frac{1}{6} \Sigma y_i \sin (x_i + \alpha)$ respectively $B = \frac{1}{6} \Sigma y_i \sin 2 (x_i + \beta)$.

Hence the parameters A, B, α and β can be computed from the observations y_i.

Summary.

In this paper a method to give the seasonal birth rhythm in parameters is described, by which the comparison of the birth frequency curves can be made more exactly. To determine the deviations of the monthly percentages from the mean we have chosen as curve

$$y = A \sin (x + \alpha) + B \sin 2(x + \beta).$$

The following examples have been chosen:

1. the birth rhytms of Switzerland during the decennaries from 1870 to 1947;

2. the rhythms of the live and still births of Switzerland during the periods 1932–40 and 1941–47;

3. the birth rhythms of several parts of the U.S.A. over the periods 1922–29 and 1933–40.

At the end we gave the derivation of the mathematical equation of the composed sinusoïde.

Résumé.

Nous décrivons une méthode pour donner le rythme des naissances en paramètres, par laquelle la comparaison des courbes des fréquences peut se produire plus exactement. Pour déterminer les déviations des pourcentages mensuels de la moyenne nous avons choisi comme courbe $y = A \sin (x + \alpha) + B \sin 2(x + \beta)$.

Les exemples suivants ont été choisi:

1. les rythmes des naissances de la Suisse pendant les périodes décennales de 1870 jusqu'à 1947;

2. les rythmes des naissances vivantes et mortes en Suisse pendant 1932–40 et 1941–47;

3. les rythmes des naissances des parties différentes des Etats-Unis pendant 1922–29 et 1933–40.

A la fin nous avons donné la dérivation de l'équation mathématique de la sinusoïde composée.

Zusammenfassung.

Durch die gemachten Ausführungen wird eine Methode angegeben, den Geburtenrhythmus während der einzelnen Jahreszeiten in Parametern darzustellen, durch welche der Vergleich der Geburtsfrequenzkurven genauer angestellt werden kann. Um die Abweichungen der monatlichen Prozentsätze von der Durchschnittsziffer zu bestimmen, haben wir folgende Kurve gewählt:

$$y = A \sin (x + \alpha) + B \sin 2 (x + \beta).$$

Folgende Beispiele wurden ausgewählt:

1. Der Geburtenrhythmus in der Schweiz in den Jahrzehnten von 1870–1947.

2. Der Rhythmus der Lebendgeburten und Totgeburten in der Schweiz während der Jahre 1932–1940 und 1941–1947.

3. Der Geburtenrhythmus in verschiedenen Teilen der Vereinigten Staaten während der Jahre 1922–1929 und 1933–1940.

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